A Dissertation on

A STUDY OF PROGNOSTIC SIGNIFICANCE OF MICROALBUMINURIA IN NONDIABETIC PATIENTS WITH RECENT ISCHEMIC CEREBROVASCULAR STROKE

Dissertation Submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

with partial fulfillment of the regulations

for the award of the degree of

M.D. GENERAL MEDICINE

BRANCH-I

COIMBATORE MEDICAL COLLEGE,
COIMBATORE
APRIL 2015

CERTIFICATE

This is to certify that this dissertation in **"A STUDY OF PROGNOSTIC SIGNIFICANCE OF MICROALBUMINURIA IN NONDIABETIC PATIENTS WITH RECENT ISHCEMIC CEREBROVASCULAR STROKE**" was a work done by **Dr. M. KAVITHA,** under my guidance during the academic year 2012-2015. This has been submitted in partial fulfillment of the award of M.D. Degree in General Medicine (Branch-1) by the Tamil Nadu Dr. M.G.R. Medical University, Chennai-600 032

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Dissertation Topic : A STUDY OF PROGNOSTIC SIGNIFICANCE OF MICROALBUMINURIA IN NON DIABETIC PATIENTS WITH RECENT ISCHEMIC CEREBROVASCULAR STROKE.

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Page count:	120
Word count:	12,382
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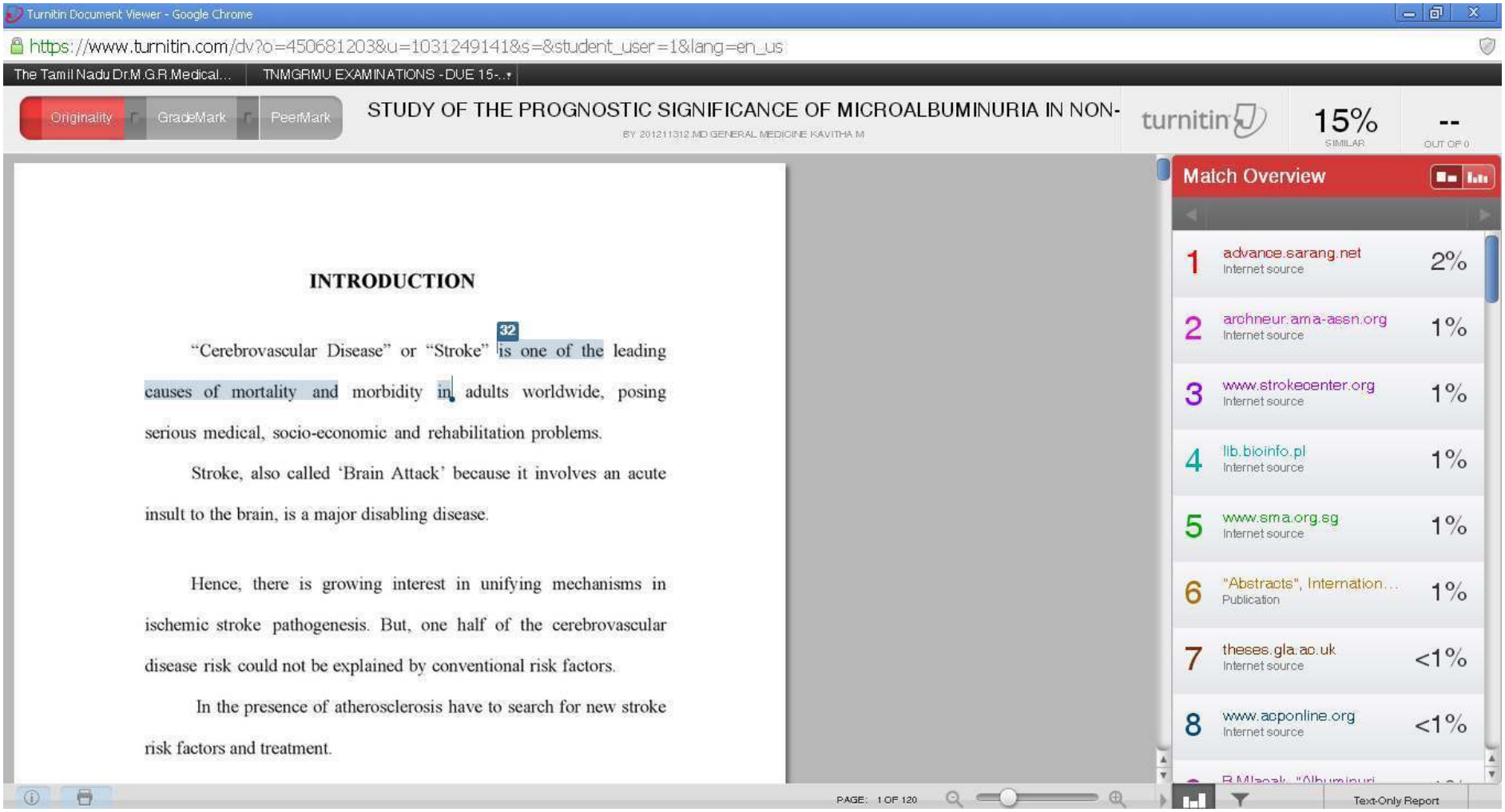
INTRODUCTION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INTRODUCTION
"Cerebrovascular Disease" or "Stroke" is one of the leading causes of mortality and morbidity in adults worldwide, posing serious medical, socio-economic and rehabilitation problems.
Stroke, also called 'Brain Attack' because it involves an acute insult to the brain, is a major disabling disease.
Hence, there is growing interest in unifying mechanisms in ischemic stroke pathogenesis. But, one half of the cerebrovascular disease risk could not be explained by conventional risk factors.
In the presence of atherosclerosis have to search for new stroke risk factors and treatment.
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I solemnly declare that this dissertation entitled **"A STUDY OF PROGNOSTIC SIGNIFICANCE OF MICROALBUMINURIA IN NONDIABETIC PATIENTS WITH RECENT ISHCEMIC CEREBROVASCULAR STROKE"** was done by me at Coimbatore Medical College and Government General Hospital during the academic year 2012-2015 under the guidance and supervision of **Prof. Dr. C. MANOKARAN. M.D.,** dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University, towards the partial fulfillment of requirement for the award of M.D. Degree in General Medicine (Branch-1).

Place : Coimbatore **Dr. M. Kavitha**

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ACKNOWLEDGEMENT

I wish to express my sincere thanks to our respected Dean **Dr. S. REVWATHY. M.D., DGO., DNB.,** for having allowed me to conduct this study in our hospital.

I express my heartfelt thanks and deep gratitude to the Head of the Department of Medicine, Prof. **Dr. KUMAR NATARAJAN. M.D.,** and my guide **Prof. Dr. C. MANOKARAN. M.D.,** for his generous help and guidance in the course of the study.

I am extremely grateful to Prof. **Dr. ISAAC CHRISTIAN MOSES M.D**., and **Dr. K. THIRUVARUTCHELVAN, M.D., D.M., (NEURO)** for his valuable help and cooperation and allowing me to use institutional facilities.

I sincerely thank all Professors and Asst. Professors **Dr. K. GANESAMOORTHY. M.D., Dr. K. JAMUNARANI. M.D., Dr. A. AKILA. M.D., Dr. S. RAMKUMAR. M.D., and Dr.S SELVAMANI. M.D.,** for their guidance and kind help.

My sincere thanks to all my friends and post-graduate colleagues for their whole hearted support and companionship during my studies.

I thank all my **PATIENTS**, who formed the backbone of this study, without whom this study would not have been possible.

Place: **Dr. M. KAVITHA**

Date:

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LIST OF ABBREVATIONS:

ACE	Angiotension converting enzyme
Bp	Blood pressure
CNS	Central nerous system
CT	Computer tomography
DBP	Diastolic blood pressure
DEH	Duration of Essential hypertension
ECG	Electrocardiography
ECHO	Echocardiography
FBS	Fasting blood sugar
H/o	History of
HDL	High density lipoprotein
HTN	Hypertension
IHD	Ischemic heart disease
JGA	Juxta glomerular apparatus
JNC	Joint National Committee
LVH	Left ventricular hypertrophy
MA	microalbuminuria
Nacl	Sodium chloride
NIDDM	Non insulin dependent diabetes mellitus
NS	Non significant

O2	Oxygen
SBP	Systolic blood pressure
Sr. Cr	Serum creatinine
TC	Total cholesterol
TIA	Transient ischemic attack
TSH	Thyroid stimulating hormone
UAE	Urinary albumin excretion
UK	United kingdom
VWL	Von Willebrands factors
WBC	White Blood Cell

INTRODUCTION

"Cerebrovascular Disease" or "Stroke" is one of the leading causes of mortality and morbidity in adult worldwide, posing serious medical, socio-economic and rehabilitation problems.

Stroke, also called 'Brain Attack' because it involves an acute insult to the brain, is a major disabling disease.

Hence, there is growing interest in unifying mechanisms in ischemic stroke pathogenesis. But, one half of the cerebrovascular disease risk could not be explained by conventional risk factors.

In the presence of atherosclerosis have to search for new stroke risk factors and treatment.

The inflammatory like C-reactive protein, intercellular adhesion molecule-1, lipoprotein associated phospholipase A2, increased WBC count, Chlamydia pneumoniae, Helicobacter pylori and Cytomegalovirus; Homocysteine; Renin angiotensin system; Tissue factor; Fibrinogen; Lipoprotein (a); Small dense LDL; etc., have been proposed as new risk factors for stroke.[4] One more addition to the growing list is 'Microalbuminuria'

Microalbuminuria has been associated with many disease entities like diabetic nephropathy, hypertension with left ventricular hypertrophy and renal insufficiency, etc.

But, there was little information regarding microalbuminuria as an independent risk factor for stroke or as a predictor of stroke outcome.

With the availability of sensitive and relatively inexpensive methods for detection of microalbuminuria, many studies were conducted in different parts of the world to determine the potential use microalbuminuria, as a marker of stroke risk and outcome in non-diabetic population.

Microalbuminuria is a marker for kidney disease and endothelial dysfunction, may be associated with global vascular risk.

Microalbuminuria is a marker of abnormal vascular permeability and its presence considered as kidney notice for increasing cerebrovascular risk.

It is considered as an indicator of increased mortality in DM, SHT, acute MI.

It is an independent risk factor for stroke or as a predictor of stroke outcome.

Microalbuminuria may be a marker for early development of atherosclerosis and a possible linkage between microalbuminuria and atherothrombotic stroke mechanisms.

DEFINITION :

Microalbuminuria is urinary excretion of albumin in the rate of 30-300mg/day or an albumin creatinine ratio of 2.5-25 mg/mmol in males and 3.5-25mg/mmol in females.

Study included all patients admitted in CMCH diagnosed with first Ischemic stroke which is confirmed by CT scan brain within first 24 hours of onset of symptoms

The severity of neurological deficit was measured by Scandinavian Stroke Scale on the day of admission.

The urinary albumin excretion was measured by using spot urine collection and by Micral test.

The patients were re-examined after 6 weeks for activities of daily living using Barthel Index.

Measuring microalbuminuria seems to be a reliable indicator of stroke outcome after 6 weeks of the stroke attack.

AIMS AND OBJECTIVES

- To estimate the presence of microalbuminuria in non-diabetic recent ischemic stroke patients.
- To evaluate the prognostic significance of microalbuminuria in these non-diabetic recent ischemic stroke patients.

REVIEW OF LITERATURE

ISCHAEMIC STROKE DEFINITION

Stroke

WHO defines stroke as "the rapidly developing clinical symptoms and/or signs of local [at times global] disturbance of cerebral functions, with symptoms lasting for more than 24 hours or leading to death with no apparent cause other than that of vascular origin" [Hatano, 1976].[5]

Transient Ischaemic Attack (TIA)

TIA, per se, does not impose any lasting burden on the individual or the society.

But it serves as a 'warning signal' for later occurrence of stroke and thus, may form the basis of a 'high risk' prevention strategy.

Reversible Ischaemic Neurological Deficit [RIND]

RIND defines an event characterized by neurological deficits that lasts more than one day but disappears within 7 days.

Stroke in Evolution

It describes a progressive neurological deficit developing over a few hours or days, which evolves to completed stroke after a few hours or days.

Completed Stroke

It is the term applied to the temporal profile of the stroke syndrome in which the deficit is prolonged and often permanent causing demonstrable parenchymal changes.

Small Vessel Stroke

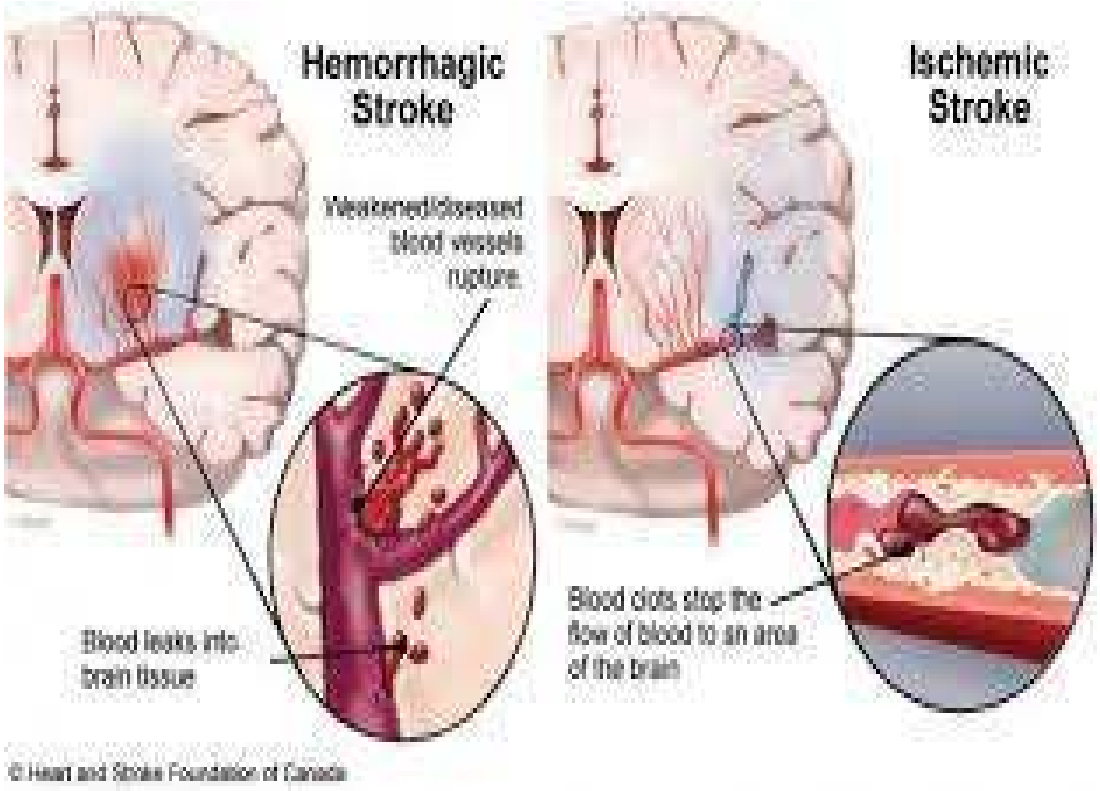
It is the infarction following atherothrombotic or lipohyalinotic occlusion of a small artery [30 - 300 mcm] in the brain [lacunar infarction].

CAUSES OF ISCHEMIC STROKE

1. Thrombosis (a locally formed blood clot which obstructing the blood vessel)
2. Embolism
3. Systemic hypoperfusion
4. Venous thrombosis

Figure-1

Image of Hemorrhagic and Ischemic Stroke



CLASIFICATION;

Hachinske and Norris Classification

Presumed Stroke Presumed TIA

Anatomic classification:

a) By vascular supply - Carotid.

Vertebrobasilar.

b) By location

Supratentorial - lobar. Ganglionic / Thalamic.

Infratentorial - Cerebellar. Brainstem.

Etiologic classification:

a. By result

- Cerebral Infarct - Arterial.

Arteriolar.

Venous.

- Cerebral hemorrhage - Parenchymal

Subarachnoid.

A. Management classification:

- TIA and minor stroke.

- Major stroke.
- Deteriorating stroke.
- Young stroke.

By cause

Ischaemia - Embolism.

- Extra cranial vascular disease.

Hemorrhage - Hypertension.

Amyloid Angiopathy.

Vascular malformation.

Aneurysm

Oxfordsire stroke sub classification;

a. Total anterior circulation syndrome

b. Partial anterior circulation syndrome

c. Lacunar syndrome

d. Posterior circulation syndrome

Figure-2

Cortical vascular teritory

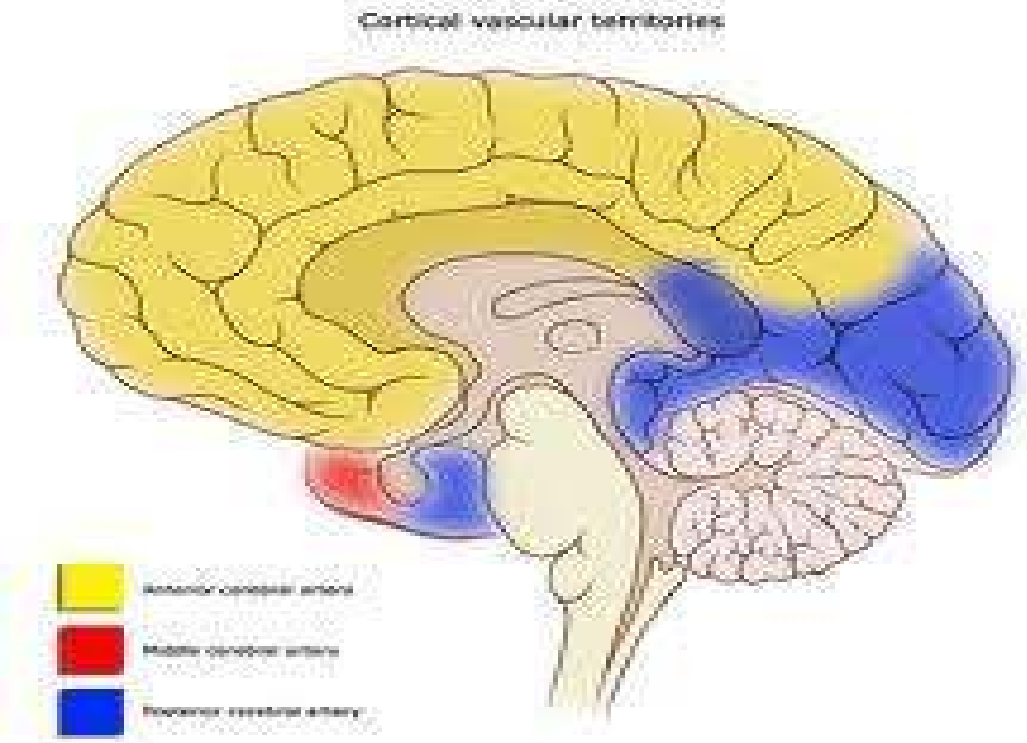
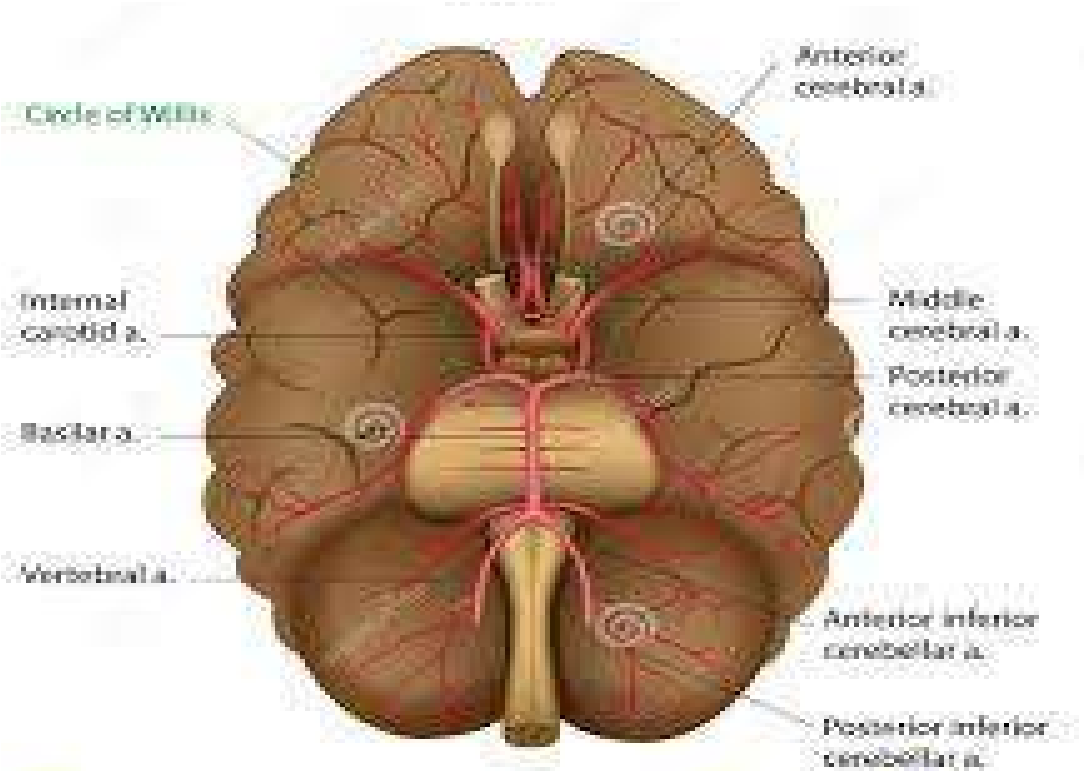


Figure-3

Blood Supply of the Brain



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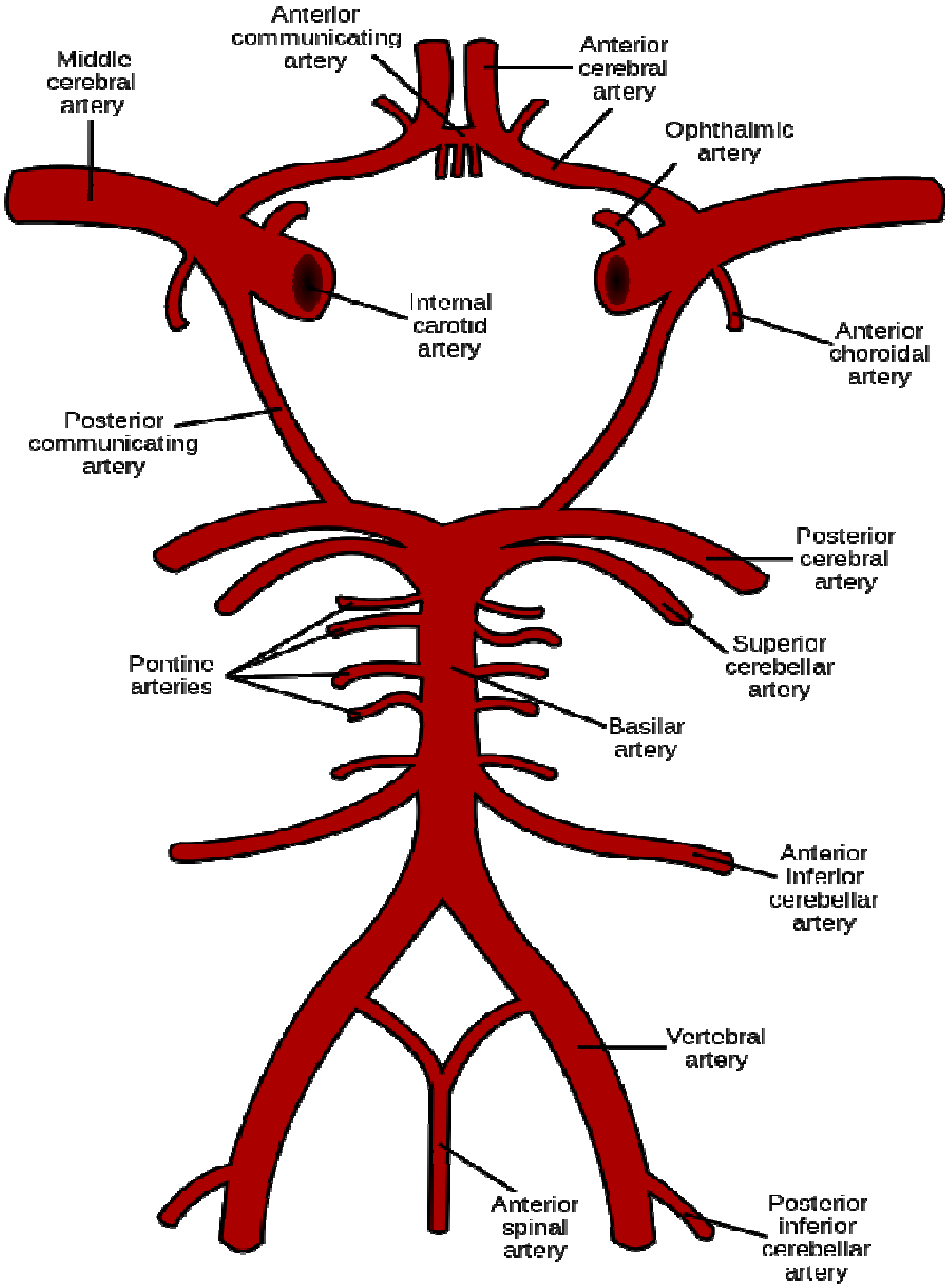
Circle of Willis



FACTORS FAVOURING BLOOD SUPPLY TO THE ISCHEMIC BRAIN TISSUE

Collateral circulation;

It helps to improve the affected area of brain.so, if colletral circulation is good, outcome will be better.

Systemic circulation;

The blood pressure in the systemic circulation is an important factor to maintain cerebral perfusion pressure and cerebral auto regulation.

Systemic hypotension can result in global cerebral ischemia.

FACTORS UNFAVOUR THE OUTCOME OF ISCHEMIC STROKE

1. HYPER COAGULABLE STATE
2. HYPERTHERMIA
3. HYPERGLYCEMIA
4. HYPOGLYCEMIA
5. HYPOTENSION
6. HEMORRHAGIC TRANSFORMATION

CEREBRAL BLOOD FLOW

- Normal cerebral blood flow-60ml/100g/min
- The cerebral auto regulatory mechanism maintains cerebral blood flow.
- It maintains systemic circulation in the range of 60-150mmHg
- CBF reduction during ischemia results in local vasodilatation and opening of collaterals
- Irreversible neuronal injury occurs in CBF, of <10ml/100gm of tissue/min

ISCHEMIC PENUMBRA

The ischemic area is surrounded by an area of decreased perfusion. This area is called as the ischemic penumbra where auto regulation is in effective.

WINDOW OF OPPORTUNITY

The critical time period in which area of brain tissue is at risk is called window of opportunity. The neurological deficits partly or completely reversed, if reperfusion of the ischemic tissue is achieved in within this period.

NEURONAL DEATH

Death of neurons after injury takes places by two processes

1. coagulation necrosis
2. apoptosis

Coagulation necrosis;

Cell death without inflammatory response in the surrounding cells is called as coagulation necrosis

Apoptosis;

Programmed cell death due to ischemia is called as apoptosis. Activation of silent suicidal proteins in the nucleoli, causes autolytic process and cell death.

INTRACRANIAL HEMORRHAGE

Accumulation of blood within skull vault is called ICH

Intra axial- blood inside the brain, extra axial hemorrhage- blood inside the skull vault but out side the brain.

Extra axial hemorrhage

1. Epidural
2. Subdural
3. subarachnoid

EPIDEMIOLOGY

Worldwide annual incidence of stroke is 0.2-2.5/1000 population. Worldwide prevalence rate of stroke is 500-600/1,00,000 population.

About 15 million people affected by CVA every year worldwide.

About one third of CVA patients ends in permanent disability. About one third of CVA patient die.

In Europe the stroke incidence is high in men than women. Indian stroke morbidity and mortality study shows in Dalal 2007 study prevalence is 55.6/100000 in all age group.

WHO study shows 0.63 million death due to stroke in 2005.

A. Incidence and prevalence of stroke in India

The first study were conducted in vellore. In the first phase (1968-69), a population of 2,58,576 in and around Vellore was surveyed to detect the prevalent cases of stroke. The main observations made during this study are:

1. Two year prevalence rate of stroke - 84 per 1,00,000 population.

2. Annual incidence of stroke - 13 per 1,00,000 population.

The second study was carried out as a part of WHO collaborative study in Rohtak, Haryana between 1971 and 1974. The study made the following observations:

1. Crude prevalence rate - 44 per 1,00,000 population.
2. Annual incidence of Stroke - 33 per 1,00,000 population.

Subsequent study done in Gowribidanur in Karnataka in South India found the prevalence rate of stroke to be 52/1,00,000.

In Eastern India, a neuroepidemiological study in rural Bengal found prevalence of stroke to be 126/1,00,000 and in Chottanagapur in Bihar it was 103/100,000.

The stroke prevalence in Metropolitan city of Mumbai has been reported as high as 245/100,000.

In a smaller study in New Delhi, the crude prevalence of stroke has been reported to be 125/100,000 population.

Mortality due to stroke

The stroke mortality rate is 73 per 100,000.

EPIDEMIOLGY OF MICROALBUMINURIA

Microalbuminuria is defined as levels of albumin between 30 - 300 mg per day (equivalent to 20 to 200 µg/minute in a timed overnight urine collection, 20-200 mg/L on spot urine specimen or ACR 2.5 to 25 mg/mmol in males or 3.5 to 25 mg/mmol in females),

Table.1.

Timed urine collection			Spot morning urine specimen			
Albuminuria Level	**24-hour albumin excretion (mg/day)**	**Overnight albumin excretion (µg/min)**	**UAC (mg/L)**	**Albumin-to-creatinine ratio**		
				Gender	**mg/mmol**	**mg/g**
Normal	< 30	< 20	< 20	Male	< 2.5	< 20
				Female	< 3.5	< 30
Microalbuminuria	30 - 300	20 - 200	20 - 200	Male	2.5 - 25	20 - 200
				Female	3.5 - 25	30 - 200
Gross proteinuria	>300	>200	>200	Male	>25	>200
				Female	>25	>200

- **Detection of microalbuminuria**

A lot of dipsticks (such as Clinitek Microalbumin and Chemstrip Micral-Test) are available to detect microalbuminuria [49] These strips are inexpensive and simple to use in clinical setting but may not precise and accurate.

There are Several laboratory techniques available for quantitative measurement of microalbuminuria [50]. These techniques have high specificity for detection of albumin. The most frequently utilised techniques for are immunoassays. Non-immunological techniques for quantifying microalbuminuria are also available. These tests are mainly based on chromatographic techniques such as size-exclusion high performance liquid chromatography (HPLC) [50]

- **Confounders of microalbuminuria screening**

There are a lot of confounding factors affect microalbuminuria screening and leads to false-positive results . In healthy individuals strenuous exercise may increase albumin level in the urine, even above the threshold of microalbuminuria [51]

The mechanism for exercise-induced temporary microalbuminuria is not completely established. It may be because strenuous exercise causes increase in glomerular filtration pressure which leads to increase in glomerular permeability [51]

Another possible confounder is Urinary tract infection (UTI) .So the therapeutic guidelines recommend to exclude the samples that show positive evidence of UTI and recommend to submit the mid-stream specimen of urine (MSSU) forbacteriology [52]. Fever, upright position for a long time, pregnancy and menstruation are the other confounder of microalbuminuria screening [53].There is high variability in the excretion of albumin in the urine in these conditions. Therefore, re-examination of additional samples after a suitable time gap is recommended

Table.2.

Confounders	
Upright posture	Pregnancy
Exercise	Menstruation
Fever	Haematuria
Symptomatic UTI	Renal impairment
Heavy protein diet	Hyperglycemia
Inflammation	Hypertension
Infections (e.g. hepatitis)	Heart failure

: Examples of factors associated with increased urinary albumin excretion

Screening methods and number of samples

There is a general consensus that the gold standard of microalbuminuria screening is 24-hour urine collection [54]However, it will be difficult for the individual to completely compliant with this method so this approach is rarely utilised. One of the simpler and more easily accomplished way of timed microalbuminuria measurement is Overnight albumin excretion rate [55] One advantage of overnight urine collection is more stable albumin excretion because of minimum movement during bedtime [56]

More commonly used methods are measuring urinary albumin concentration (UAC) or ACR on random samples [57] or first morning voids. [58] The easiest and most convenient method for the patients and the practitioners is the random spot urine collection. For collection of first morning urine sample, the patient is instructed to empty the bladder before going to bed and to collect the first void after awaking up from sleep. These methods are minimally affected by biological variations and they should ideally reflect the real magnitude of albumin excretion in the urine.

Various studies have recently tried to identify the best method for microalbuminuria screening. In a subset analysis of the PREVEND

study, the researchers compared UAC and ACR, both from first morning void and random sample; the purpose of the analysis was to identify which test better replicated 24-hour urine collection [54]. First morning ACR sample was equivalent to 24-hour urine collection with similar variability and prevalence. Another subset analysis of the PREVEND study revealed that ACR from first morning samples was correlated with 24-hour urinary albumin excretion (UAE) in predicting cardiovascular morbidity and all-cause mortality after 7.5 years follow-up [59]. 700 type II diabetics participated in the RENAAL trial were followed for 3.4 years [59]According to the study ACR was the best predictor for renal outcomes. From these studies the reliability of ACR in detecting clinically relevant microalbuminuria is clear.

First morning samples measured by ACR had better reliability in microalbuminuria screening because of their exhibition of low variability. When there is high urine volume the UAC tends to be reduced, as the amount of creatinine filtered over time is relatively constant the ACR corrects for variability in urine excretion [60]. Urine from first morning void usually reflects the real magnitude of urinary albumin excretion without any influence from the confounding factors such as exercise.

According to Several international guidelines recommendation, repeated samples are necessary for diagnosing microalbuminuria (2 out of 3 samples should be positive) [61]. The repeated samples are recommended in order to overcome the effect of any possible confounders of microalbuminuria screening. However, this is difficult to achieve in clinical settings, hence the diagnosis of microalbuminuria in the majority of studies (especially in hypertension) has been based on single samples.

- **Epidemiology of microalbuminuria**

In different populations with the same clinical condition the prevalence of microalbuminuria varies significantly. This variability might be due to several factors such as the measurement methods, threshold used, instruments or extent of co-morbidities in the study population (e.g. in hypertension; mild, moderate or severe) (table 1-2).

PREVALENCE OF MICROALBUMINURIA IN GENERAL POPULATION:

Indian scenario

Hitha B,Pappachan J M,Balachandran pillai H,[62]: In 150 cases of essential hypertension studied, 40 (26.6%) patients had microalbuminuria. It was significantly higher in those with longer

duration and greater severity ($p<0.001$ in each) , older age($p<0.001$), adverse lipid profile ($p<0.01$) and higher BMI ($p<0.04$). There was increased risk of recent stroke, hypertensive retinopathy and left ventricular hypertrophy (29.33%). Gender and history of smoking did not pose any risk for microalbuminuria.

Sharma V K,Dubey T N,Jain R K [63]: In 50 cases of essential hypertension 12 had microalbuminuria. Among 8 newly detected 1 (12.5%) had microalbuminuria, 25% upto 10 years duration of disease and 50% more than 10 years. 12% with stage 1 and 47% with stage 2 had microalbuminuria. Hence prevalence of microalbuminuria in essential hypertension was 24% and found a strong correlation with severity and duration of hypertension.[2]

Sabharwal R K,Parduman singh,, [64]: In 174 cases of essential hypertension studied , 58(33.3%) had microalbuminuria. The prevalence was 34% in males and 30.7% in females. No correlation was found between BMI and albumin excretion and also with duration of hypertension. Prevalence of microalbuminuria in non-smokers and non-alcoholics was 20%. The prevalence in smokers, alcoholics and both alcoholics and smokers was fond to be 35%, 42%, and 41%. The high prevalence of microalbuminuria demands the establishment of screening

for microalbuminuria and implementation of specific intervention methods.

The prevalence of microalbuminuria varies according to ethnicity. Microalbuminuria is more common in black and Asian populations compared with whites. A comparison between South Asian and white European populations living in the UK revealed that microalbuminuria is significantly more common in Asians (31% versus 20%) [65]. In this study, there were no differences between the two populations in terms of age, sex or blood pressure levels. Another study compared UAE in African Caribbeans, South Asians and white Europeans [66].

The prevalence of increased UAE was higher in African Caribbeans than in South Asians and Europeans. In a cohort of 6801 subjects from different Asian countries (China, Korea, Indonesia, Philippines, Singapore, Malaysia) the prevalence of microalbuminuria was 39.8%[67].

However, in that study, urinary albumin detection was performed by semi-quantitative dipsticks and more than 30% of the involved subjects had strong family history of cardiovascular or metabolic disease. This may partially explain the high prevalence of microalbuminuria. In a large epidemiological study based on diabetic

subjects attending primary care clinics, hypertensive Hispanic subjects and non-hypertensive Asians showed prevalence of microalbuminuria higher than that in Whites subjects [68]

The relation between prevalence of microalbuminuria and gender is not clear. According to some studies males have higher microalbuminuria prevalence [69], others reported no gender differences [70] In the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) which involved type 1 diabetics showed that UAE was associated with male gender and this association was because of central obesity (measured as waist-hip ratio- WHR) [71]. When the prevalence was adjusted for WHR, no association between gender and UAE was observed. The Prevalence of microalbuminuria was significantly higher in females in the EPIC-Norfolk study (14.1% versus 8.4%, $P<0.001$) [72]

Prevalence in subjects with diabetes mellitus

In management of diabetes, microalbuminuria screening is recommended by the majority of clinical guidelines [73]. Many studies addressed the prevalence of microalbuminuria in diabetic individuals. In order to examine the development of microalbuminuria, The Oxford Regional Prospective Study recruited type I diabetics aged under 16

years [74]. According to the study the prevalence of microalbuminuria was 25.7% and 50.7% after 10 years and 20 years respectively. Around 30% of adults with type I diabetes develop microalbuminuria within 18 years after diagnosis[75]

The United Kingdom Prospective Diabetes Study (UKPDS 64) included 5097 type II diabetes patients (67% newly diagnosed) from different ethnic origins in their study and followed them for 20 years in order to find the progression of diabetic subjects to nephropathy[76]. At baseline, the prevalence of microalbuminuria of the study population was nearly 7% and after the prevalence 5, 10 and 15 years were 17%, 25% and 28%, respectively.

Prevalence of microalbuminuria in subjects with hypertension

Although a number of studies have attempted to define the prevalence of microalbuminuria in essential hypertension, the exact prevalence is still unclear. The estimated prevalence of microalbuminuria in hypertensive subjects from varios studies ranges from 4.7% to 58.4% [77]. A longitudinal study involving 1,041 young (18-45 years) hypertensives (stage 1) demonstrated that prevalence of microalbuminuria was 6% of the study population detected using the 24-hour method [78]. In this particular study the low prevalence of

microalbuminuria mainly because of the young age of the participants (as microalbuminuria tends to be more common among older subjects [79]) and also due to the early stage of hypertension of the subjects.

The urine dipstick method seems to overestimate the prevalence detection of microalbuminuria. For instance, in Germany in a large cohort of non-diabetic hypertensive subjects about 32% had microalbuminuria [80] In this study, the diagnosis of microalbuminuria was based on two positive urine dipsticks (Micral-Test) out of three. In the i-SEARCH global study the highest prevalence of microalbuminuria (58.4%) was observed from 26 countries Almost 21,000 subjects participated in this clinic-based study.The overall prevalence of microalbuminuria was high among participating countries, with rates of 53 to 71% in some developing countries. However, one of the major limitation of this study was that the diagnosis was based on a single urine specimen measured using urine strips. Also, the majority of the study population was diabetic and above 60 years of age and which were the causes for the high prevalence of microalbuminuria.

In summary, the reported prevalence of microalbuminuria has been limited by, under-precision caused by single screening, measurement method, too many restrictions on population tested or

small sample size. The reliable information on microalbuminuria in hypertension is limited and thus, the prevalence remains to be elucidated.

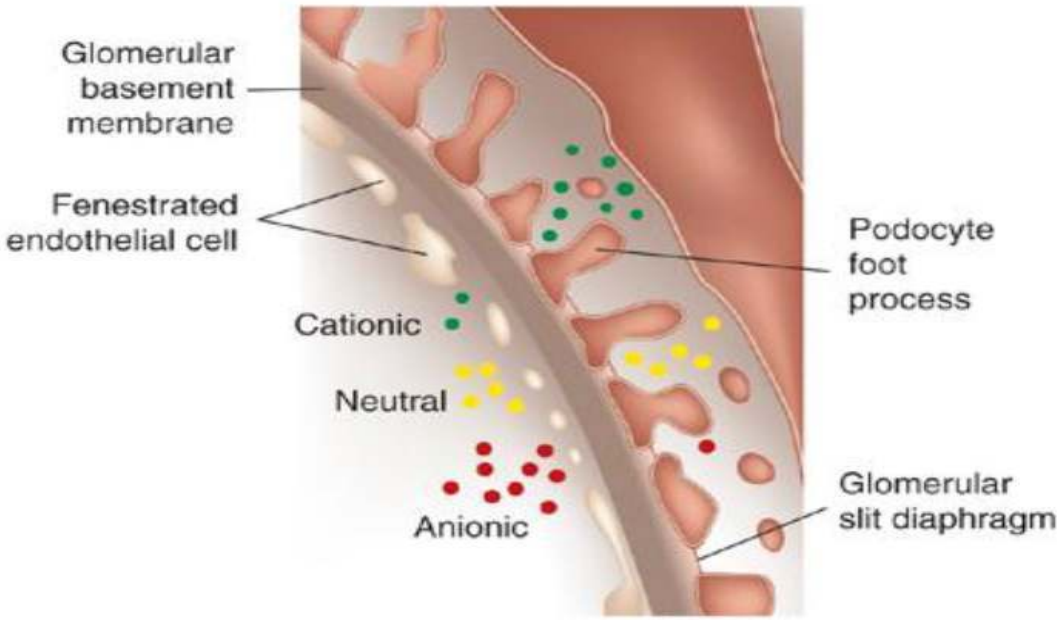
Pathogenesis of microalbuminuria

The pathophysiological mechanisms underlying the proteinuria in hypertensive individuals are not completely understood. Various mechanisms have been proposed. Most of these mechanisms involve alteration in the renal haemodynamics and endothelial changes [81]

The glomerular filtration barrier consists of three layers; the endothelium, the glomerular basement membrane and podocyte foot processes. Each layer plays important role in preventing some molecules from being excreted as an ultrafiltrate.

Figure.5

Glomerular Basement Membrane



As mentioned before, the maintainence of the glomerular pressure is mainly by afferent arteriole. In hypertension, in order to protect the kidney from the high hydrostatic pressure produced by high blood pressure the afferent arteriole tends to constrict. Specific cells in the distal convoluted tubule also regulates this feedback mechanism mediated by constricting the afferent arteriole to maintain GFR when the volume of filtrate is high [82].Impairment of this autoregulatory process which leads to hyperfiltration and passage of albumin into urine is induced by prolonged high blood pressure [82]. This hypothesis is

supported by an experimental animal model, in which partial nephrectomy causes hyperfiltration in the remaining nephrons in order to maintain GFR, which in turn led to glomerular hypertension and proteinuria [83]

It has been postulated that impairment of glomerular permeability is also a major contributor in the pathophysiology of microalbuminuria [84]. The changes in the structure of the glomerular filtration barrier led to alteration of glomerular permeability. Glomerular filtration barrier compoed of three layers, they are endothelium covered by anionic glycoprotein (glycocalyx), glomerular basement membrane andpodocyte foot processes [85]. This barrier prevents some molecules from escaping to the lumen of Bowman capsule. As the glycocalyx is negatively charged it repells the albumin as it is also negatively charged. Therefore, any structural changes could translate into passage of larger amount of albumin in the urine. Impairment of the podocytes [86,87] and glycocalyx [88] have been shown in diabetic patients with microalbuminuria and subjects with hypertensive nephrosclerosis [89]

Impaired function of the renin-angiotensin aldosterone system (RAAS) has also been implicated. Angiotensin II has been found to contribute in the sclerosis of the podocytes leading to excretion of large

molecules including albumin[91]. Activation of angiotensin II type 1 receptors leads to an increase in the production of reactive oxygen species (ROS) and different inflammatory mediators which mediate endothelial injury in the kidney and in the blood vessels[92,93]. There is significant reduction in microalbuminuria and several biomarkers of inflammation and oxidation by inhibition of angiotensin receptors using pharmacological approaches and drugs with putative anti-oxidant properties, which supports this hypothesis [94,95]

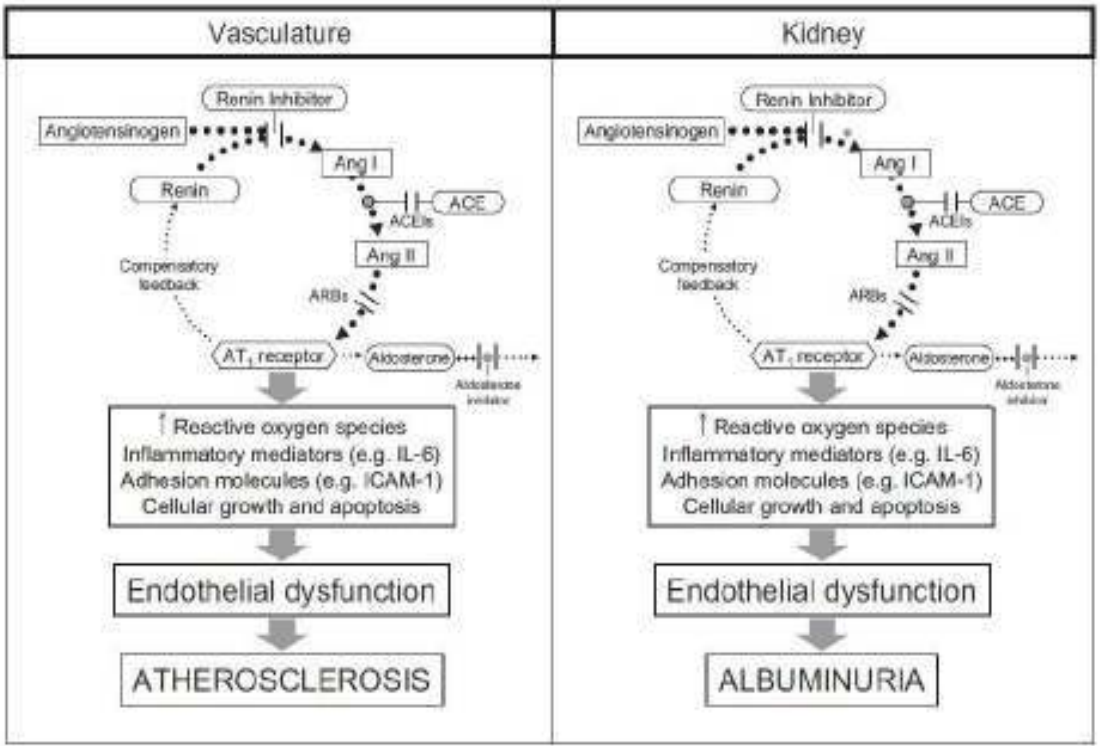


Figure. 6

Simple illustration of mechanisms by which malfunction of RAAS could mediate albuminuria and atherosclerosis. Adapted with permission from [90]

It has been suggested that microalbuminuria is a marker of generalised endothelial dysfunction and it also reflects the systemic vascular abnormalities which may explain the association of microalbuminuria with different cardiovascular diseases [96]. Cottone et al.[97] have shown that UAE is correlated well with levels of various adhesion molecules that are involved in atherosclerosis of blood vessels.

All mechanisms mentioned previously could mediate microalbuminuria. As a result of increased blood pressure there is alteration in renal hemodynamics which leads to increase in glomerular permeability. In addition, defects in renin-angiotensin system leads to increased oxidative stress and high levels of inflammatory markers which leads to endothelial dysfunction which in turn causes increased permeability

Association of microalbuminuria with diseases and risk factors

Over the last decade, our understanding of the role of microalbuminuria as an important independent risk factor for metabolic

and cardiovascular morbidities has expanded exponentially. An increasing body of evidence suggests that microalbuminuria is emerging as a useful tool for predicting several diseases[98] This is because microalbuminuria is reflecting the more complex vascular changes which occurs in the body. However, among the clinicians the awareness of the association of various diseases with microalbuminuria is still poor. A survey among 1700 clinicians (general practitioners, cardiologist and diabetologists) in five European countries was conducted by Haller and colleagues[99] to evaluate the awareness of importance of microalbuminuria in clinical practice. The vast majority (over 93%) of clinicians was aware of the association between microalbuminuria and impairment of renal function. There was extremely limited awareness of the association of microalbuminuria with abnormalities in other organs.

For example, among participated clinicians in the UK, only 16%, 10%, 9%, 8% and 4% were aware of the relation between microalbuminuria and eyes, macrovascular,cardiac, microvascular and brain complications, respectively. As screening of microalbuminuria is easy and relatively inexpensive this finding is disappointing and also of the result of the screening may guide the clinician to identify individuals who are at high risk for cardiovascular complications.

Microalbuminuria and high blood pressure

There is plausible association between high blood pressure and increased UAE. One of the proposed mechanisms and also one of the most frequently reported predictors of microalbuminuria is High blood pressure [100]. In MAGIC (Microalbuminuria: A Genoa Investigation on Complications) study [101] and Gubbio Population studies [102] there were direct relationships between high blood pressure and microalbuminuria. These are the studies that aimed to characterise microalbuminuria in non-diabetic subjects with hypertension. This relation was also supported by a large cross-sectional study involving 4 subgroups; 1) diabetic patients with severe atherosclerosis,2)non diabetic with severe atherosclerosis, 3)diabetic with mild atherosclerosis and 4)non-diabetic with mild atherosclerosis [103]. In this study, albuminuria was significantly associated with high bloodpressure (even below the threshold level for the definition of hypertension) in all four groups

The relationship between increased blood pressure and albuminuria has also been reported in studies which using 24-hours blood pressure monitoring There were positive correlations between microalbuminuria and 24-hour SBP, DBP and pulse pressure in a small group of subjects who are not having any evidence of cardiovascular or

metabolic abnormalities [104] This relationship was also evident in 1) diabetic patients [105], 2) hypertensive subjects with end organ damage [106], 3)resistant hypertension [107] and 4) general hypertension population [108]. These findings are of particular importance because now ambulatory blood pressure is being considered as the gold standard for the diagnosis of hypertension and it also helps in the identification of subjects with true refractory hypertension[109] and therefore, it will represent the most reliable data for the association with microalbuminuria.

People who are lacking the normal blood pressure reduction during sleeping (non-dippers) are associated with increased UAE [110]. UAE was related to 1) non-dipping pattern in a cohort of recently diagnosed hypertension[111], 2) in subjects with untreated hypertension[112] and 3) those with resistant hypertension [107]

Microalbuminuria and renal function

Microalbuminuria is best recognised for its the association with deterioration in kidney fnction. Microalbuminuria may be present at an early stage of renal disease, even when eGFR is normal [113] For the prediction of end stage renal disease (ESRD) , recent recommendations suggest the use of albuminuria in addition to eGFR [114,115] In a study

which involved almost 66,000 patients and they were followed for ten years. The result of the study revealed both eGFR and albuminuria were independent predictors for ESRD. This association was also reported recently in subjects with high cardiovascular risk and in diabetics who are followed for 10 years[116,117] Combining albuminuria and eGFR screening identified hypertensives at high risk of cardiovascular mortalities and morbidities in a prospective cohort study[118]. Increased albuminuria was a strong predictor for progression to ESRD in a Canadian cohort study with a large number of patients (> 900,000)[119]. 917 non-diabetic hypertensives with normal renal function were followed for a median of 11.8 years in a sub-analysis of the MAGIC study, [120] More than one-third of subjects who developed chronic renal insufficiency had increased urine albumin excretion at baseline compared with 7% in the control group. The relation of microalbuminuria with renal outcome was independent of eGFR or other confounders. Likewise in a retrospective study, hypertensive subjects were followed for 7 years and decline in creatinine clearance and increased cardiovascular events was associated with microalbuminuria [121]in non-diabetic hypertensive subjects Regression. or significant reduction of UAE (defined as reduction exceeds 50%) by drugs were associated with better renal outcomes [122]. These findings clearly

suggest that microalbuminuria provides more information than that provided by eGFR in prediction and identification of impaired kidney function. Therefore, routine screening for people at high risk for chronic diseases should include albuminuria screening in order to prevent or delay the progression to ESRD.

Microalbuminuria and cntral nervous system

- **Stroke risk**

Results of various cross-sectional and prospective studies suggest that microalbuminuria is prevalent in patients with recent acute stroke and may predict future stroke events [123]. In a prospective case-control study involving patients who are at high risk for developing stroke (hypertension, diabetes, transient ischemic attack (TIA) or ischaemic heart disease) and patients with recent acute stroke (within a week), the prevalence of microalbuminuria in those with stroke was significantly higher than that in the high-risk group (29% versus 10%) [124]. During a mean follow-up period of 1.5 years, almost 15% of the high-risk group and one-fifth of subjects with recent stroke were developed vascular events. In subjects with albuminuria new onset vascular events were more frequent even after adjusting other risk factors such as diabetes, high blood pressure, and cigarette smoking.

The Losartan Intervention For Endpoint reduction (LIFE) examined the association of cardiovascular events with microalbuminuria in 8206 hypertensives with LVH [125]., the study revealed that for every 10-fold increase in UAE after follow up of the subjects for a median of 4.8 years and the risk for stroke increased by 50%. However, this result has some limitations. The limitations are 1)microalbuminuria was detected using only one specimen ,2)did not include any measure to exclude those with UTI and 3) the study was performed in high-risk population and it is uncertain whether the same pattern may be observed in patients without LVH.

EPIC-Norfolk study, a general population study in which the subjects were followed up for 7.2 years, revealed that there was 50% increased risk for stroke in subjects with microalbuminuria [126]. The hazard ratio for the association between stroke events and microalbuminuria was greater than that for some traditional risk factors such as body mass index (BMI), total cholesterol; SBP was revealed by a Cox multiple regression models. In this study the detection of microalbuminuria was based on single random sample method which may overestimate albuminuria prevalence as discussed previously.

The relation of microalbuminuria with stroke was evaluated by a meta-analysis involving twelve studies with more than 48,000 patients. The above said studies involved different populations with or without different co-morbidities such as, hypertension, cardiovascular disease, prior stroke or diabetes mellitus. stroke events was strongly associated with microalbuminuria. Comparing the individuals with normoalbuminuria, subjects with microalbuminuria had a 90% greater risk for developing future stroke incidents.

In the survey by Haller et al. [100], the association of brain abnormalities with microalbuminuria was the least recognised association. This indicates that clinicians may miss an non-invasive and easy technique for identifying individuals at high risk of cerebrovascular diseases.

Cognitive decline and cerebrovascular changes

The largest body of evidence for the interaction between cognitive function and albuminuria (microalbuminuria and proteinuria) comes from the the Telmisartan Randomized AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease (TRANSCEND) and Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) [127]. More than 28,000 patients suffering

from diabetes mellitus or vascular diseases participated in these trials. Cognitive function was assessed by using a 30-point Mini–Mental State Examination (MMSE) at baseline and after 5 years to evaluate the degree of dementia. Subject people with albuminuria at baseline had lower MMSE scores (less than 24) and they also had higher odds for reduced cognitive function. Similarly, during the study those who developed albuminuria had increased odds for cognitive impairment. One of the major drawbacks of the study is the population studied. The conclusions cannot be extended to those without vascular abnormalities or diabetes as these disorders may also interact with cognitive decline.

Ravera and colleagues [128] investigated the association of microalbuminuria with subclinical cerebrovascular changes in a small number of untreated hypertensive subjects (11 with microalbuminuria and 11 with normoalbuminuria) with no other clinical neurological disorders. Using magnetic resonance imaging, the researchers found that there was greater prevalence of cerebral lacunar infarcts in subjects with microalbuminuria. In a cohort of elderly subjects in Japan, microalbuminuria was correlated with cerebral small vessels disease (SVD) [129]. In addition, in subjects with microalbuminuria there were increased prevalence of ischaemic lacunar lesions and white matter hyperintensity. Another cross-sectional study carried out in 2316 elderly

subjects showed that dementia and mild cognitive impairment were significantly related to microalbuminuria. [130]., revealed microalbuminuria was significantly related to deep or infratentorial cerebral microbleeds investigated by neuroimaging in 285 hypertensives who were not having any evidence of severely reduced renal function ,stroke, TIA or [130],.Proteinuria was strongly related to Brain microbleeds in patients who had stroke or TIA events [131].

These findings are important for various reasons.

1) Several brain abnormalities such as cognitive decline, age-associated disorders and stroke has been increasingly linked with cerebral SVD [132].

2) White matter hyperintensities, which are possibly due to SVD-induced ischaemia, have been shown to predict cognitive decline, stroke, and mortality [133]

3) The association between brain microbleeds and mortality [134], neurological disorders such as Alzheimer's disease and has been suggested.

The identification of cerebrovascular changes like SVD, cerebral microbleeds and white matter lesions are time-consuming, expensive

and also they are not routinely requested investigations (ultrasonography or special neuroimaging). Microalbuminuria screening possibly serve as an appropriate tool for identifying people at high risk for cerebrovascular complications.

Microalbuminuria and cardiovascular abnormalities

A growing body of evidence links microalbuminuria with cardiovascular system abnormalites. As mentioned earlier, microalbuminuria is a marker of generalised endothelial dysfunction which is a key factor for various cardiovascular diseases such as, myocardial infarction, CHD, heart failure, atherosclerosis and hyperlipidemia

Ischaemic heart disease risk

A number of studies suggest the prognostic value of microalbuminuria for ischaemic heart diseases [135]. 9 % of the Subjects with untreated hypertension and high-normal blood pressure in the Danish MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) project had future ischemic heart disease when were followed for ten years [136]. The prevalence of microalbuminuria in patients developing ischaemic heart disease was higher than that in the control group. After adjusting for known factors

such as blood pressure, lipids, gender and BMI the relative risk for developing ischaemic attack associated with microalbuminuria was 3.5. UK population-based study confirms these findings where future episodes of CHD with hazard ratios of 1.36 and 1.59, respectively were predicted by microalbuminuria and gross proteinuria following acute myocardial infarction the prognostic value of microalbuminuria for short and long-term outcomes has also been investigated. Berton et al. [137] studied albuminuria in patients admitted for acute myocardial infarction and compared findings with a control group (those admitted for suspected myocardial infarction but did not meet the diagnostic criteria). UAE that was measured by 24-hour urine collection was higher both on the day of admission and after 2 days when compared with the control group. But, participants in the control group were younger (i.e. not age-matched) and also had fewer cardiovascular co-morbidities that biased the comparison. Another study revealed that increased UAE was present in more than one-third of hospitalised patients with acute myocardial infarction [138] . A strong predictor for myocardial infarction complications including mortality was increased UAE

A study involving 175 non-diabetic patients with acute myocardial infarction was followed for 3 years aiming to identify factors that were associated with subsequent cardiovascular events or death [139].

Microalbuminuria, that was measured by timed overnight urine collection on the third day after the event proved to be an independent predictor for both endpoints. Similar findings have also been shown in a larger non-diabetic cohort in which cardiovascular complications following myocardial infarction episodes were higher than in those patients without microalbuminuria [140] Thus, in patients with myocardial infarction, increased UAE might identify those at increased risk for complications. future complications may be lowered More vigorous treatment.

Left ventricular hypertrophy and structural changes

The relation between increased UAE and LVH in a population with essential hypertension have been investigated by The LIFE study [141] nearly 9200 hypertensive subjects with evidence of LVH on electrocardiography (ECG) but no evidence of recent stroke, myocardial infarction ,low left ventricular ejection fraction (less than 40%), or severe kidney impairment participated. Even possible confounders such as high blood pressure, increased age and diabetes were adjusted. Both microalbuminuria and proteinuria strongly associated with LVH .

Data from the Hypertension Genetic Epidemiology Network (HyperGEN) revealed that albuminuria has been associated with

increased left ventricular size (on echocardiography) in both normotensive and hypertensive individuals; reduced ejection fraction has been seen only in microalbuminuric hypertensive subjects [142] Various Electrocardiological abnormalities such as intraventricular conduction defects, rhythm abnormalities, left axis deviation and ventricular repolarisation alterations were also associated with microalbuminuria [143].

It has been proven recently that in hypertensive subjects with ventricular diastolic impairment, microalbuminuria is related with increased ventricular remodelling, stiffness and increased levels of NT-proBNP which is a marker for heart wall stress [144] On the other hand, reduction in eGFR did not reveal an association with such changes in the myocardium. This means that microalbuminuria gave information in addition to that offered by the classical marker of kidney disease. The significance of such findings is that microalbuminuria could recognize those with high risk for progression to heart failure. It could help to discover pharmacological agents with properties to prevent such progression.

Congestive heart failure (CHF)

An association of microalbminuria with CHF is expected as its association with other cardiac outcomes such as CHD and myocardial infarction. This association was established in the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) trial[145]. Two thousand three hundred and ten patients with heart failure took part in the programme. Albuminuria was identified in 41% of the patients (30% microalbuminuria and 11% gross proteinuria). Similar prevalences were observed after excluding diabetes and hypertension. In this patient population, albuminuria was useful functional predictor for mortality and further degeneration in the myocardium in the studied population.

The prevalence of gross proteinuria and microalbuminuria in a small group of subjects who participated in the ALiskiren Observation of heart Failure Treatment (ALOFT) study was 11% and 33%, respectively . Albuminuria was detected by dipstick in an Asian population and it was associated with CHF with preserved left ventricular ejection fraction and predicted future death [146]. In hypertensive subjects with LVH in the LIFE study, albuminuria was correlated with twofold increase in risk of incident heart failure [147]

In the general population, data from the Multi-Ethnic Study of Atherosclerosis (MESA) which involved 6,800 individuals with different ethnic background determined that albuminuria was the strongest predictor of new-onset CHF [148] .Though the follow-up period (4 years) was too short for estimation of such an outcome, this study is particularly interesting for several reasons. Firstly, it explained the incidence of severe cardiac outcome in apparently healthy subject without clinically detectable cardiovascular disease. Secondly, the study included subjects from four different ethnicities; Caucasians, black,Asian and Hispanics. At the end, the researchers demonstrated the association between heart failure and microalbuminuria even after adjusting for traditional risk factors. This observation recommends that albuminuria is important in risk stratification for severe cardiac outcomes.

Vascular diseases

Arterial stiffness that was measured by pulse wave velocity (PWV) has been reported in subjects with microalbuminuria[149]. This condition is a risk factor for future cardiovascular events [150] . Loss of arterial elasticity leads to increase in the force of contractions of the heart which in turn might lead to LVH and severe complications [150,151].

In subjects without hypertension or diabetes, arterial stiffness was associated with microalbuminuria after adjusting for possible confounders [152] In small groups of untreated hypertensive subjects, the prevalence of microalbuminuria in those with arterial stiffness that was measured by carotid / femoral arteries PWV or ambulatory arterial stiffness index was notably higher [153]. The association remained vital in adjusted regression models.

Microalbuminuria has been also related with coagulation abnormalities. A sub-analysis from the PREVEND study described an increased incidence of venous thromboembolism in subjects with microalbuminuria [154]. The incidence rate was 0.40% per year for those with UAE ≥ 30 -300 mg per day compared with only 0.12% per year for those with UAE <15 mg per day (P<0.001). A recent post-hoc analysis of the PREVEND study indicated that microalbuminuria was also related to increased risk for recurrent venous thromboembolism [155]

A direct relationship between albuminuria and atherosclerosis has been noted in many studies. Both these conditions share a common pathological mechanism, endothelial damage. In a Norwegian study, a direct relation between ACR and de novo formation and progression of atherosclerotic plaque in the carotid artery has been reported in subjects

without diabetes.Moreover, microalbuminuria revised the formation and the progression of early marker of atherosclerotic lesion in the carotid artery (calcification) in clinically health individuals who participated in the MESA study [156]Increased carotid intima-media thickness, a risk factor for atherosclerosis, was also reported in hypertensive subjects with microalbuminuria [157]

RISK FACTORS FOR STROKE

1. Age:

Increasing age results in increased incidence of stroke. Stroke is found to be 25 times more common in people aged 75-84 years than in people aged 45-54 years.

2. Sex:

There is slight male preponderance in middle and old age.

TIA and thrombotic are more common in male

Embolic stroke more common in female.

Stroke morbidity is high in males

In various studies male to female ratio is high(5.5;1 according toaganial et al. and 3.2;1)

3. Blood Pressure:

Hypertension is strongly associated with stroke risk, the risk being present for both systolic and diastolic BP.[13,14] The age adjusted relative risk for cerebrovascular disease in hypertension was 3.1 for men and 2.9 for women.[15]

4. Smoking:

It is established that there is dose-response relationship, affecting both sexes in all age groups. Even passive smoking increases the stroke risk.

The number cigarettes smokes per day is directly proportional to CVA risk.

As per Framingham study, 16 year followup shows CVA is three times more common in smoker than nonsmoker.

5. Blood lipids:

The relationship between blood lipids and stroke is much weaker than that for coronary artery disease, but serum lipoprotein (a) is found to be predictive.[17]

6. Diabetes Mellitus:

Patients with diabetes have double the risk of stroke compared to non-diabetics.[18] Stroke in diabetics is more likely to be fatal.[19]

7. Haemostatic variables:

Increased fibrinogen, raised plasma coagulant activity, reduced blood fibrinolytic activity, raised von Willebrand factor and raised haematocrit are all risk factors for stroke.[21, 22]

8. Atrial Fibrillation:

AF, acts as the most frequent cardiac source of embolism to the brain.

9. Alcohol:

Alcohol also raises the BP, [25] alters blood lipids, causes AF and cardiomyopathy and this may increase stroke risk.

10. Obesity:

Stroke risk increases particularly if the weight has been gained in middle age or has fluctuated substantially or compounded by hypertension and diabetes.[25]

11. Diet:

Omega-3 polyunsaturated fatty acids and less saturated fatty acid consumption may reduce stroke risk.[27] Excessive salt intake may increase blood pressure and increases stroke risk.[28] High intake of potassium reduces the stroke risk by lowering blood pressure.[29]

12. Exercise:

Reduces the risk of NIDDM, thus reducing stroke risk.

13. Non-stroke Vascular Disease:

Coronary artery disease, asymptomatic peripheral vascular disease and TIA are all associated with increased stroke risk.[31, 32]

14. Genetic Factors:

Various vascular anomalies; connective tissue disorders like Ehler-Darlos Syndrome, Pseudoxanthoma elasticum, Marfan's syndrome,

Fibromuscular hypoplasia, MVP; hematological diseases like sickle cell disease, anti-thrombin III deficiency, protein deficiency, dysfibrinogenemia; familial hypercholesterolaemia; cerebral amyloid

angiopathy; homocysteinemia; Fabry's disease; cardiac myxoma; mitochondrial cytopathy etc are associated with increased risk of stroke.[33]

CAUSES OF ISCHEMIC STROKE[34]

Causes of ischemic stroke

Common causes

Thrombosis

- Lacunar stroke
- Large vessel Thrombosis
- Dehydration

Embolic occlusion

- Artery-to-artery
    - Carotid bifurcation
    - Aortic arch
    - Arterial dissection
- Cardioembolic
    - Atrial Fibrillation
    - Mural thrombosis
    - Myocardial infarction
    - Dilated cardiomyopathy

Valvular lesions

- Mitral Stenosis
- Mechanical valve
- Bacterial Endocarditis
- Paradoxical embolus
- Atrial Septal defect
- Patent Foramen ovale
- ASD
- ECHO contrast

Hypercoagulable disorders

- Protein C deficiency
- Protein S deficiency
- Anti-thrombin III deficiency
- Anti-phospholipid syndrome
- Factor V Leiden Mutation
- Prothrombin G 20210 Mutation
- Systemic malignancy

- Sickle cell anemia
- Thalassemia
- Polycythaemia vera
- Systemic lupus erythematosus
- Homocysteinemia
- Thrombotic thrombocytopenic purpura

DIAGNOSTIC APPROACH IN STROKE PATIENTS

- The rapid evaluation of patient is essential for use of time-sensitive treatments such as thrombolysis.
- An adequate history from an observer is essential.
- Once the stroke is diagnosed, a brain imaging study is necessary to determine if the cause of CVA is ischaemic or hemorrhagic.

BASIC INVESTIGATION

Hematological investigation ;

- Complete hemogram
- Hematocrit
- Prothrombin time
- Activated partial thromboplastin time
- Peripheral smear

Biochemical investigation;

- Fasting blood glucose
- Lipid profile
- Blood urea
- Sr. creatinine
- Sr. electrolytes
- Liver function tests
- Urine routine

Other investigations;

- X-ray chest
- ECG
- Echocardiography

Special investigations

- Computerized tomography
- MRI
- USG
- Doppler
- Digital subtraction angiography

TREATMENT[34]

Management includes;

- Supportive care
- Intravenous thrombolysis
- Endovascular methods
- Antithrombotic treatment
- Neuroprotection and stroke

Supportive care

To maintain perfusion to the area surrounding the infarction

Prevention of complication-

Infection

Deep vein thrombosis

Blood pressure maintenance

Good glyceamic control

Anti edema measures

Special care in cerebellar infarction

Medical support

- Protection of airway to avoid obstruction, hypoventilation and aspiration.
- Maintenance of body temperature to prevent hyperthermia.
- Maintenance of blood glucose less than 200 mg/dl and BP around 150 mmHg.
- Maintenance of nutritional status and fluid requirement.
- Watch for brain edema and treat it with mannitol.
- Bowel and bladder care, prevention of pressure sores and infections.

Thrombolysis

IV rtPA at a does of 0.9 mg/kg within 3 hours of stroke onset seems to have a role in the treatment of acute ischaemic stroke.

Table 3

Administration of intravenous Recombinant Tissue Plasminogen Activator (rtPA) for acute ischemic stroke

Indication
Clinical diagnosis of stroke.
Onset of symptoms to time of drug administration < 3 hrs.
CT scan showing no hemorrhage or significant edema.
Age > 18 years.
Consent by patient or surrogate.

Anti-platelet drugs:

Ingestion of aspirin within 48 hrs of stroke onset reduces both stroke recurrence and mortality. Agents that act at glycoprotein II b/III receptors are under trial.

Anti-coagulation:

Trials not support the use of heparin or other anticoagulants for patients with atherothrombotic stroke..

Neuroprotection:,

Excitatory amino acid pathway blockers etc., are under trial.

Rehabilitation:

It includes early physical, occupational and speech therapy.

PRIMARY AND SECONDARY PREVENTION

1. General principles

- Life style modification.
- Evaluation of patients clinical risk profile and control of risk factors like hypertension, hyperlipidemia, diabetes etc.
- Use of alternate day aspirin in high risk patients.

2. Atherosclerotic Risk factors

- Use of Angiotensin converting enzyme inhibitors and angiotensin receptor blockers.
- Use of statins.

3. Anti-platelet drugs

Aspirin, Clopidogrel and combination of Aspirin and dypridamole are used.

4. **Anti-coagulation therapy**:

Used in embolic stroke to maintain INR 2-3.

PROGNOSTIFICATION IN ACUTE STROKE [36]

The stroke outcome may be influenced by many variables:

Demographic variables

Includes age, gender and race.

Young better than in old,

married than in the unmarried,

rural areas than urban areas and in those discharged home than in those transferred to long term care hospitals.

General Medical Characteristics

HT,DM,CAD,AF,OBESITY,DYSLIPIDEMIA,SEDENTARY LIFE STYLE are associated with increased risk of recurrent stroke and thereby would influence long term survival.

Comorbidities like heart disease, COPD, peripheral vascular disease, Parkinson's disease, polyneuropathy, osteoarthritis etc have a direct effect on functional recovery and compound the patient's disabilities.

Lesion related variables

Survival is better in infarction than in hemorrhage.

Anterior circulation infarcts have higher risk of death and so also intracerebral or subarachnoid hemorrhage.

Occurrence of coma at stroke onset reflects severity and is an important predictor of 30-day survival.

Severity of paralysis, urinary and bowel incontinence also adversely influence the outcome.

Specific therapy intervention

Better management of respiratory and cardiac problems in acute phase may result in decreased mortality.

Biochemical variables

Protein C and S have been found to be decreased in some patients with ischemic stroke and predict adverse outcome.

Lipoprotein (a) is found to be an independent risk factor for arteriovascular disease.

Recent studies have suggested that presence of microalbuminuria is associated with poor stroke outcome.

OUTCOME PREDICTION IN INDIVIDUAL PATIENTS

The scoring system used in this are;

1. National Institute of Health Stroke Scale.
2. Canadian Stroke Scale.
3. Scandinavian Stroke Scale.
4. Orpington Prognostic Scale.
5. Fugl-Meyer Assessment.
6. Barthel Index.
7. Communication Index.

Of these, the features of the scoring systems used in this study are:

Table-4

Scandinavian Stroke Scale

Function	Score	Prognostic score	Long term score
Consciousness:			
Fully conscious.	6		
Somnolent can be awaked to full consciousness.	4		
Reacts to verbal command, but not fully conscious.	2		
Eye movement			
No gaze palsy.	4		
Gaze palsy present.	2		
Conjugate eye deviation.	0		
Arm, motor power			
Raises arm with normal strength.	6		
Raises arm with reduced strength.	5		
Raises arm with flexion in	4		

elbow.			
Can move, but not against gravity.	2		
Paralysis.	0		
Leg, Motor power			
Normal strength.	6		
Raises straight leg with reduced strength.	5		
Raises leg with flexion of knee.	4		
Can move, but not against gravity.	2		
Paralysis.	0		
Orientation			
Correct for time, place and person.	6		
Two of these.	4		
One of these.	2		
Completely disorientated.	0		
Speech			
No aphasia.	10		
Limited vocabulary or	6		

incoherent speech.			
More than yes / no, but not longer sentences.	3		
Only yes/no or less.	0		
Facial palsy			
None/dubious.	2		
Present.	0		
Gait			
Walks 5 M without aids.	12		
Walks with aids.	9		
Walks with help of another person.	6		
Sits without support.	3		
Bedridden / wheel chair.	0		
Maximal Score	0-52		

Table 5 Barthel Index[38]

Activity	Score			
Feeding O = unable. 5 = needs help cutting, spreading butter etc. or requires modified diet. 10- independent.	0	5	10	
Bathing O = dependent. 5 = independent (or in shower).	0	5		
Grooming O = needs to help with personal care. 5 = independent face / hair / teeth/ shaving (Implements provided).	0	5		
Dressing O = dependent. 5 = needs help but can do about half unaided. 10 = independent (including button, zips, laces etc).	0	5	10	
Bowels O = incontinent (or needs to be given enemas). 5 = occasional accident. 10 = continent	0	5	10	
Bladder O = incontinent or catheterized and unable to manage alone 5= occasional accident 10 = continent.	0	5	10	

Toilet use O = dependent. 5 = needs some help but can do something alone. 10 = independent (on and off, dressing, wiping).	0	5	10	
Transfers (bed to chair back) O = unable, no sitting balance. 5 = major help (one or two people, physical) can sit. 10 = minor help (verbal or physical). 15 = independent.	0	5	10	15
Mobility (on level surfaces) O = immobile or < 50 yards. 5 = wheel chair independent, including corners > 50 yards. 10 = walks with help of one person (verbal or physical) > 50 yards 15 = Independent	0	5	10	15
Stairs O = unable. 5 = needs help (verbal, physical, carrying aids). 10 = independent.	0	5	10	
Total	**[0 - 100]**			

STUDIES RELATING MICROALBUMINURIA and ISCHAEMIC STROKE

Although microalbuminuria is associated with clinical risk factors for stroke including diabetes, hypertension, aging, history of myocardial infarction and left ventricular hypertrophy there was little information regarding microalbuminuria being independent risk factor for stroke or as predictor of stroke outcome. But, in recent times, several studies have been conducted to ascertain any relationship between microalbuminuria and ischaemic stroke.

Damsgaard EM et al followed 216 people who had been selected as control subjects for diabetics during a systematic screening for diabetes mellitus among all people aged between 60-74 years, living in municipality of Fredericia, Denmark, between Feb 1981 and Dec 1987. Extensive clinical and biochemical examination found median urinary albumin excretion rate of 7.52 mcg/ min. 8 of those with a rate below the median died compared to 23 with a rate equal to or greater than the median. The median albumin excretion rate in the 31 who died was 15 mcg/min and cardiovascular disease was the main cause of death in both groups.[67]

1. Yudkin et al used Islington Diabetes Survey in 1988 to study urinary albumin excretion and found that urinary albumin excretion had skewed distribution with maximum rate of 191.9 mcg/min. There was significant correlation between albumin excretion rate and systolic BP, diastolic BP and 2 hour blood glucose, but not with age, sex or body mass index.[68]

2. Heikke Miettinen et al followed up cohorts of non-diabetics [n=1375] and NIDDM [n=1056] subjects in Finland between 1982 and 1990 and found elevated urinary albumin excretion in 25% non-diabetics and 58% of NIDDM patients. All case mortality was higher both in non-diabetic and NIDDM subjects with borderline or clinical proteinuria, than in those without proteinuria.[69]

3. Mlacak B et al studied the frequency of albuminuria in patients with and without diabetes (138/160) randomly selected from a stratified sample comparable with known diabetes by age, sex and profession in Metlika country, Slovenia between 1994 to 1998. The groups were examined in the same way and mortality was followed over 5 years. Albuminuria was significantly high in diabetics, peripheral arterial disease,

hypertension, coronary heart disease and hyperlipidemia. The albuminuria was frequent in those who died in the observed 5 year period.[70]

4. Nancy B. Beamer et al conducted a study in Portland Veterans Administration and Oregon Health Sciences University Hospital in Portland around 1999 and found that microalbuminuria was 3 times more prevalent in patients with recent stroke (29%) than in those with clinical risk factors for stroke (10%) and was undetectable in healthy elderly controls. During follow up period of 1.5±0.9 years, 20% of patients with recent stroke, 14% with risk factors for stroke and 0% of healthy elderly volunteers had vascular end points with events being as frequent in patients with microalbuminuria (32%) as in patients with macroalbuminuria (33%).[71]

5. Yuyun MF et al conducted a population based prospective cohort study in British population consisting of 23,630 individuals between 40-79 years, and followed them up for 7 years (1993 - 1997), with baseline albuminuria tested. A total of 246 stroke events occurred. Age adjusted incidence of stroke increased significantly across categories of baseline albuminuria. They concluded that microalbuminuria is independently associated

with approximately 50% increased risk of stroke in the general population.[72]

6. Hans. L. Hillege et al conducted PREVEND (Prevention of Renal and Vascular End Stage Disease) study in Groningen, Netherlands around 2001 and found that increased level of albuminuria was more frequent with advanced age, male sex, diabetes, hypertension, hyperlipidemia, smoking etc. Although micro and macroalbuminuria was found more frequently in diabetic and hypertensive sub group, microalbuminuria was still prevalent in 6.6% of the non diabetic, non-hypertensive subjects and independently associated with cardiovascular risk factors and morbidity.[73]

7. Turaj W et al conducted a study on 52 patients in stroke unit of Neurological Department in Jagiellonian University, Caracow, Poland within 24 hours after stroke onset (2001). Microalbuminuria was found in 24 of 52 stroke patients (46.1%) and in 5 of 37 controls (13.5%) ($p<0.05$). Patients with microalbuminuria scored lower on the Scandinavian stroke scale than patients without microalbuminuria, both on admission and later.[74]

TESTS FOR MICROALBUMINURIA

Several methods have been described for measurement of urinary albumin excretion with emphasis on unexpensive, easy to apply, rapid tests which can be used on a large scale population. The various methods used are:

Dipstick method.

Semi quantitative method.

1. 1.Chemical precipitation (Sulphosalicyclic acid trichloroacetic acid)
2. Immuno precipitation (Micral Test).

Photometric method.

Nephelometric method.

Sensitive Quantitative methods

1. Radio immuno assay.
2. Cellulose acetate, agarose gel electrophoresis.

The procedures of various important methods include the following:

Dipstick method:

Chemically impregnated dipstick contains methyl red and bromophenol blue with buffering salts. The later dissolve on contact with urine and protein in the urine lowers the pH turning it green. It was traditionally known to detect albuminuria >300 mg/L and hence not advocated for screening for microalbuminuria. But, in a study by Alfredo Pegoraro et al, they found that the combination of sulfosalicylic acid testing and chemstrips was as good as and less expensive than Micral-Test in ruling out microalbuminuria.[76]

Chemical precipitation (Sulphosalicylic acid test):

5 drops of 20% Sulphosalicylic acid is added to 3 ml of urine in one test tube. This test tube is compared with test tube of untreated urine held against a dark background, immediately and turbidity is taken to indicate proteinuria.[77]

Immunoprecipitation (Micral test):

It is based on color shift of monoclonal antibody to human albumin labelled with gold. Here Gold Labelled Optically Read Immuno Assay detects microalbuminuria. A specimen of the urine

sample passes via the wick fleece into the conjugate fleece. Any albumin present in the urine binds itself specifically to the gold labelled antibodies. Excess antibodies are bound by immobilized albumin in the capture matrix. Only antibodies bound to albumin from the urine sample can pass through the capture matrix.

These gold-labelled antibodies flow to the detection pad and turn it red. Test is performed on early morning random urine sample by immersing the strip for 5 sec and reading the result at 2 min, visually comparing with color blocks on vial (0 mg/l, 20mg/l, 50 mg/l and 100 mg/l albumin).[77]

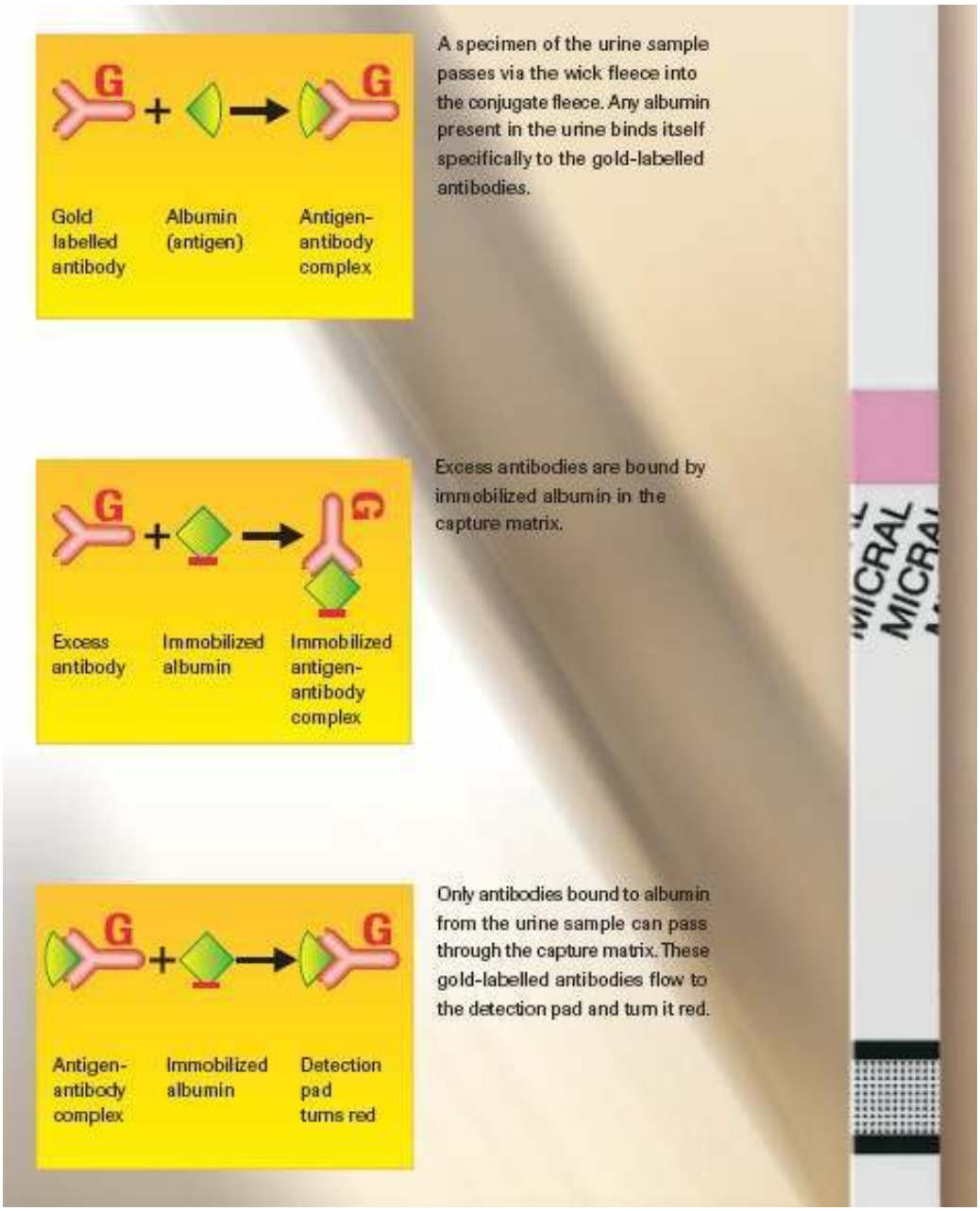


Fig. 7: Principle of Micral Test

Immerse the strip for 5 seconds as far as the two black bars

Result in 1 minute

Uncritical reading time within 5 minutes

Fig. 8: Method of using Micral Test

Radioimmuno assay:

It is the "gold standard" for estimation of albuminuria. It is a double antibody technique where albumin in the sample has to compete with the fixed amount of ^{125}I. Labelled albumin for the binding sites of the specific antibodies. Bound and free albumin is separated by addition of a second antibody immuno absorbent followed by centrifugation and decanting. The radio activity in the pellet is measured with a C-counter, Albumin concentration in the sample is inversely proportional to the radioactivity. The sensitivity for RIA method was 0.3 mg/l.

TREATMENT OF MICROALBUMINURIA

Control of Blood pressure:

Systolic BP is one of the most relevant determinants of microalbuminuria. Studies of secondary prevention have shown that blood pressure reduction effectively reduces the albumin excretion rate. Among anti- hypertensives, ACE inhibitors and Angiotensin receptor blockers seem to be particularly effective.[78] The target BP should be < 140/90 mmHg in non-diabetics and < 130/80 mmHg in diabetic patients.

Glycemic control:

adequate glycemic control can significantly reduce the risk of development of microalbuminuria and overt nephropathy in people with diabetes.

Treatment of Dyslipidaemia:

Statins modify endothelial dysfunction, inflammatory response, plaque vulnerability and thrombus formation. Their usage is known to slow progression of microalbuminuria and is associated with stabilization of UAE.[80]

Smoking cessation:

Smoking should be strongly discouraged in patients with microalbuminuria not only to retard the progression of microalbuminuria but also to guard against cardiovascular disease.

Protein restriction:

Animal studies have shown that restriction of dietary proteins intake reduces hyper filtration and intraglomerular pressure hence retarding the progression of microalbuminuria. The general consensus is to prescribe a protein intake of 0.8 g/mg/day in patients with overt nephropathy.

MATERIALS AND METHODS

Study Centre :

Coimbatore Medical College and Hospital

Study Period

From September 2013 to August 2014

Sample Size :

60 non diabetic patients with Recent ischemic stroke.

Method of Study

Prospective observational study.

Inclusion criteria

Patients of any age and both sexes with first time ischemic stroke within 24 hours of onset of symptoms, the diagnosis of stroke being established by WHO definition of stroke.

Ischemic lesion confirmed by CT Scan brain.

Informed consent obtained from all patients.

Exclusion criteria

Patients with hemorrhagic stroke.

Patients with diabetes, defined as fasting plasma glucose > 126 mg/dl or 2-hour plasma glucose > 200 mg/dl during an oral glucose tolerance test or use of antidiabetic drugs.

Patients with hypertension, defined as systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg or the use of anti-hypertensive medication.

Systemic infection including bacterial meningitis.

a) Nephropathy and abnormal urinalysis.

b) Major trauma and surgery.

c) Previous history fo stroke

- Detailed history, clinical examination and relevant laboratory investigation were done as per the proforma.
- The severity of stroke was assessed using Scandinavian Stroke Scale.

Stroke can be classified into three categories:

MILD	4
MODERATE	3-2
SEVERE	1-0

MEDICAL RESEARCH COUNCIL SCALE:

Grade 0 : No Contraction

Grade 1 : Flicker of contraction

Grade 2 : After elimination of gravity,there may be active movements

Grade 3 : Active movements against gravity

Grade 4 : Active movements against gravity and against some amount of resistance

Grade 5 : Normal power

In the selected patients, the following investigations were done.

1. CT scan brain (plain) to establish the ischemic lesion.
2. Urinalysis, to exclude hematuria, leucocyturia, glucosuria and proteinuria.

3. Serum glucose levels, blood urea, serum creatinine and fasting lipid profile,LFT were estimated.

4. ECG, chest x-ray were done to assess the cardiac status.

5. The albumin excretion rate was assessed using Micral test on early morning urine sample and expressed as --------- mg/L. Microalbuminuria was defined as urinary albumin excretion rate between 30-300 mg/L.

After discharge from the hospital, patients were re-examined 6 weeks later to measure the stroke outcome including mortality from any cause and the capacity to perform the activities of daily living (ADL) using Barthel Index.

The patients with microalbuminuria were screened for stroke risk factors and assessed for, fasting serum glucose, WBC count, total cholesterol, LDL, HDL and triglycerides.

Method of statistical analysis

The data was collected and entered in Microsoft excel. The graphs and tables were generated using Microsoft Word and Excel. The analysis of the data was done using the statistical Software namely SPSS 11.0 and Systat 8.0. Chi-square and Fisher Exact Test

were used to test the significance of proportions of predisposing Factors and presence of microalbuminuria between cases and controls. Similar tests were used to find the significance of proportion of presenting factors and age between the microalbuminuria positive and negative patients. Student t test (Two tailed) was used to test the significance of mean pattern of parameters between cases and controls and microalbuminuria positivity and negativity.

RESULTS AND ANALYSIS

Study Design

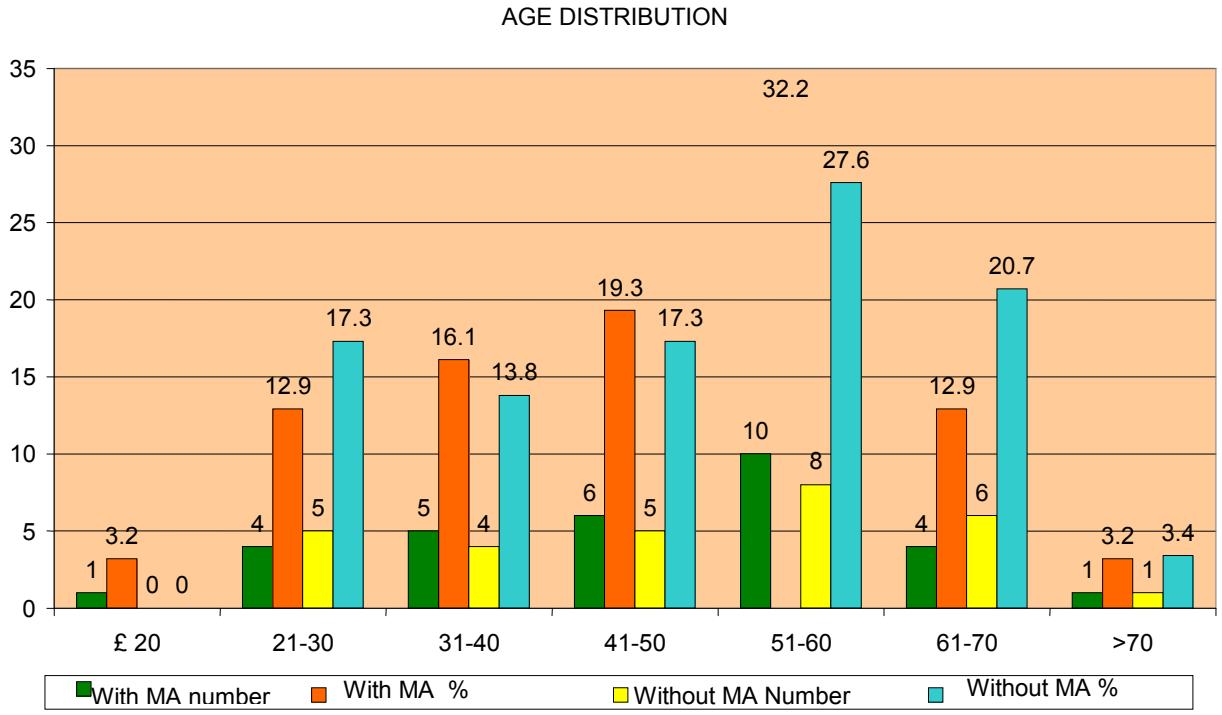
This prospective study consisting of 60 recently developed stroke patients as divided in to two groups as patients with microalbuminuria(31) and patients without microalbuminuria(29) had the following findings

Table - 6

Age distribution

Age in years	With MA		Without MA	
	Number	%	Number	%
<20	1	3.2	0	0
21-30	4	12.9	5	17.3
31-40	5	16.1	4	13.8
41-50	6	19.3	5	17.3
51-60	10	32.2	8	27.6
61-70	4	12.9	6	20.7
61-70	4	12.9	6	20.7
>70	1	3.2	1	3.4
Total	31	100.00	29	100.00
Mean ±SD	47.19±14.03		48.69±15.23	
Inference	Two groups are age matched with p=0.693			

Figure -9 Age distribution



Among the patients with microalbuminuria, the youngest patient was 19 years old and the oldest patient 77 years. The mean age was 49.94 ±15.01 years.

Among the patients without microalbuminuria, the youngest patient was 21 years and oldest patient was 74 years. The mean age was 49.00±14.77 years.

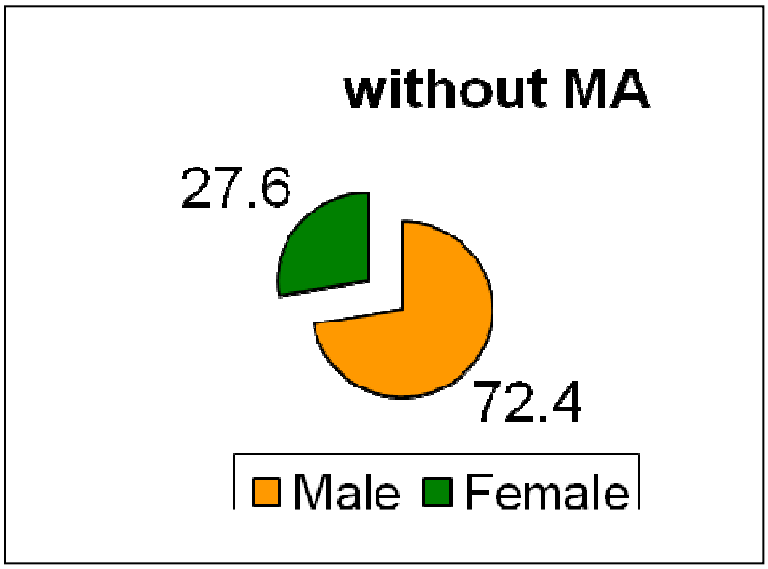
Hence the two groups were age matched with p=0.693.

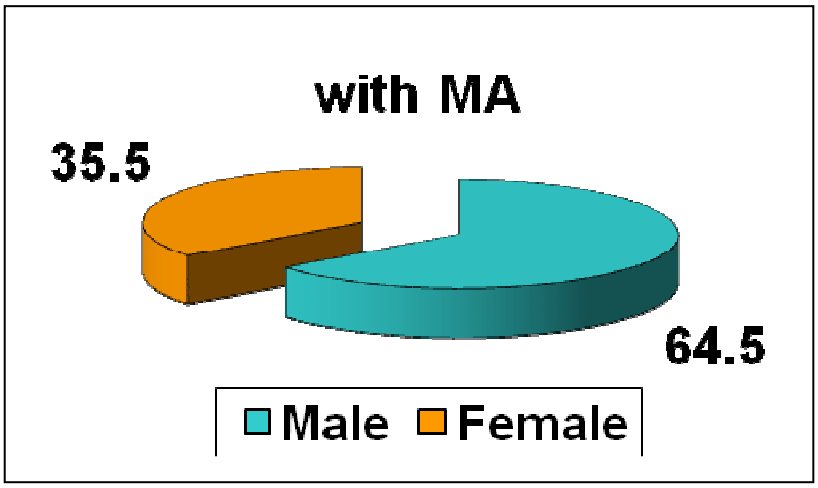
Table 7

Sex distribution

Age in years	With MA (n=31)		Without MA (n=29)	
	Number	**%**	**Number**	**%**
Male	20	64.5	21	72.4
Female	11	35.5	8	27.6
Total	31	100	29	100

Figure 10
Sex distribution





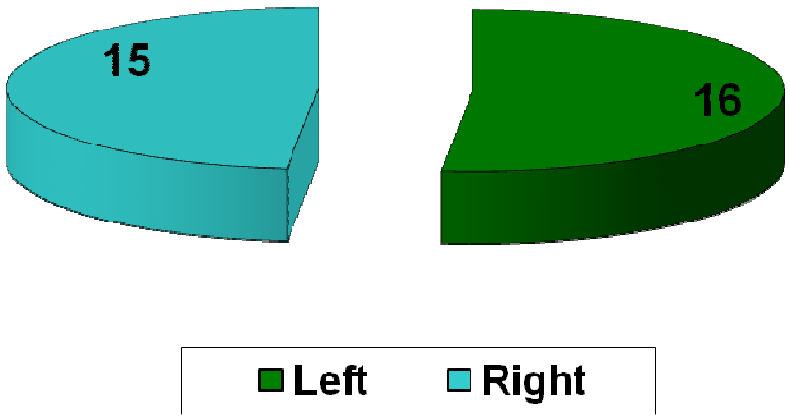
Among the patients with MA, 20 (64.5%) were male patients while 11 (35.5%) were female patients. Among the patients without MA, 21 (72.4%) were male patients and 8 (27.6%) were female patients. Hence the cases and controls were sex matched.

Table 8

Side of paucity of movements patients with microalbuminuria

Paucity of movements	With MA (n=31)	
	Number	%
Left	16	51.38
Right	15	48.62
Total	31	100

Figure 11
Paucity of Movements



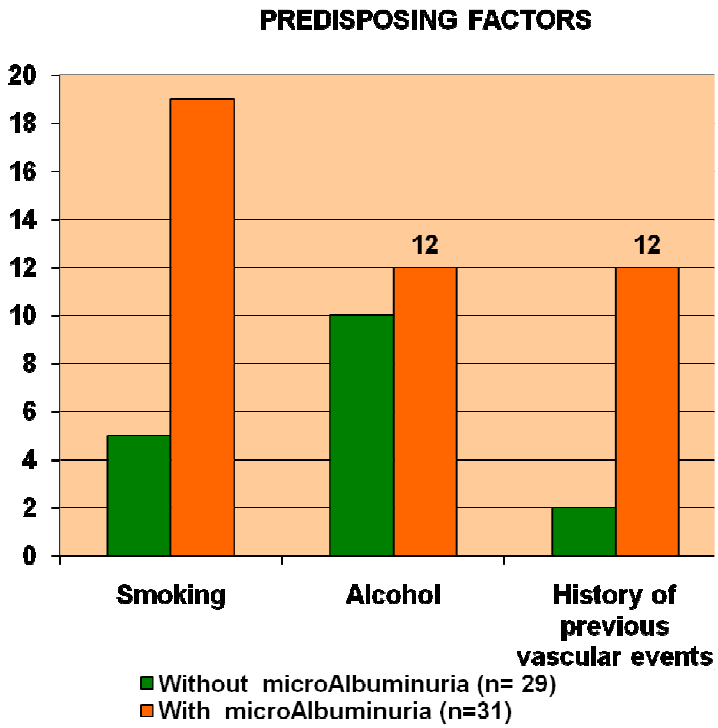
Among the patients with MA, 15 (48.62%) had right-sided hemiparesis, 16 (51.38%) had left-sided hemiparesis .

Table 9

Predisposing factors

Predisposing factors	With MA(n=31)	Without MA(n=29)	p value
Smoking	19 (61.29)	5 (17.27)	0.038
Alcohol	12 (41.4)	10 (32.3)	>.05
History of previous vascular events	12 (38.70)	2 (6.89)	0.043
Inference	The predisposing factors are statistically not similar between two groups (p<0.05)		

Figure 12



In the study population, the predisposing factors included smoking being 19 (61.29%) in patients with MA and 5 (17.27%) in patients without MA and alcoholism being 12 (41.4%) in patients with MA and 10 (32.3%) in patients without MA.

The history of previous vascular events including ischemic heart disease and peripheral vascular disease was found in 12(38.70%) of patients with MA and 2(6.89%) of patients without MA.

j

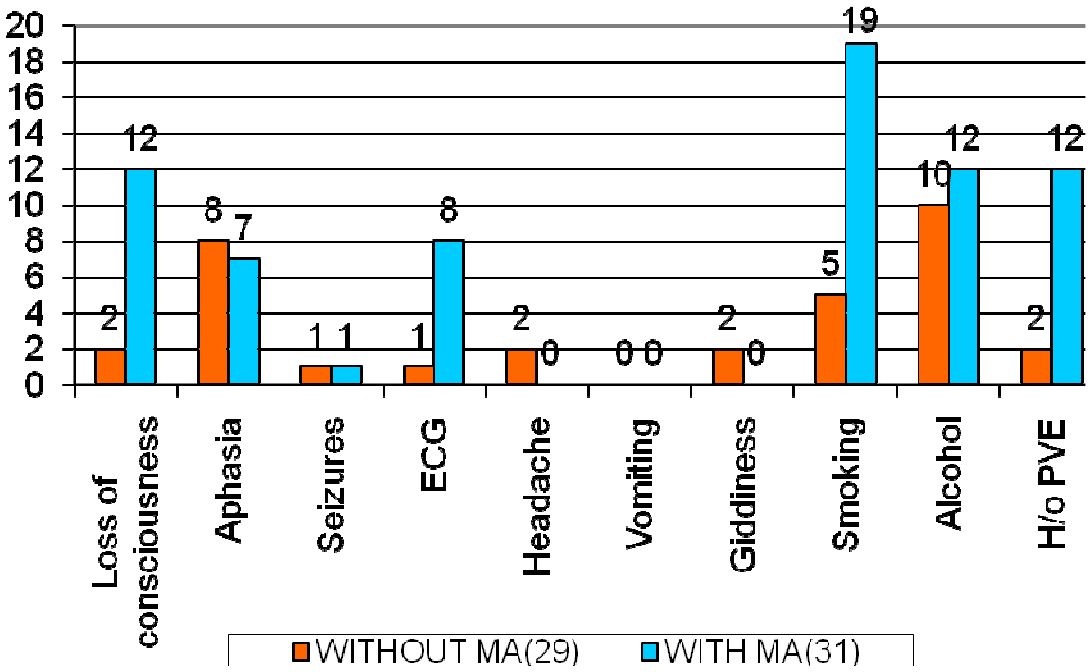
Table 10

Association of presenting factors with Microalbuminuria

S.No	Presenting factors	Microalbuminuria		Total (n=60)	p value
		Absent (n = 29)	Present (n=31)		
1.	Loss of consciousness	2	12	14	0.043*
2.	Aphasia	8	7	15	p>0.05
3.	Seizures	1	1	2	0.534
4.	ECG/IHD	1	2	3	0.036*
5.	Headache	2	-	2	p>0.05
6.	Vomiting	-	-	-	-
7.	Giddiness	2	-	2	p>0.05
8.	Smoking	5	19	24	0.038*
9.	Alcohol	10	12	22	p>0.05
10.	H/o PVE	2	12	14	0.043*

Figure – 13

Association of presenting factors with Microalbuminuria



Patients had presented with paucity of movements on one side with loss of consciousness (23.33%), aphasia (20.00%), seizures (3.33%) headache (3.33%) and giddiness (3.33%).

The loss of consciousness was more common in patients with microalbuminuria (30.70%Vs.6.89%) and reached statistically significant levels.

The history of smoking was not similar among patients with and without microalbuminuria.

History of peripheral vascular event was higher in patients with microalbuminuria (41.37% Vs 6.89%), which was statistically significant.

ECG / IHD changes of ischemic heart disease was found in 8 (25.80%) patients with microalbuminuria while 1 (3.44%) of patients without microalbuminuria and reach statistically significant level.

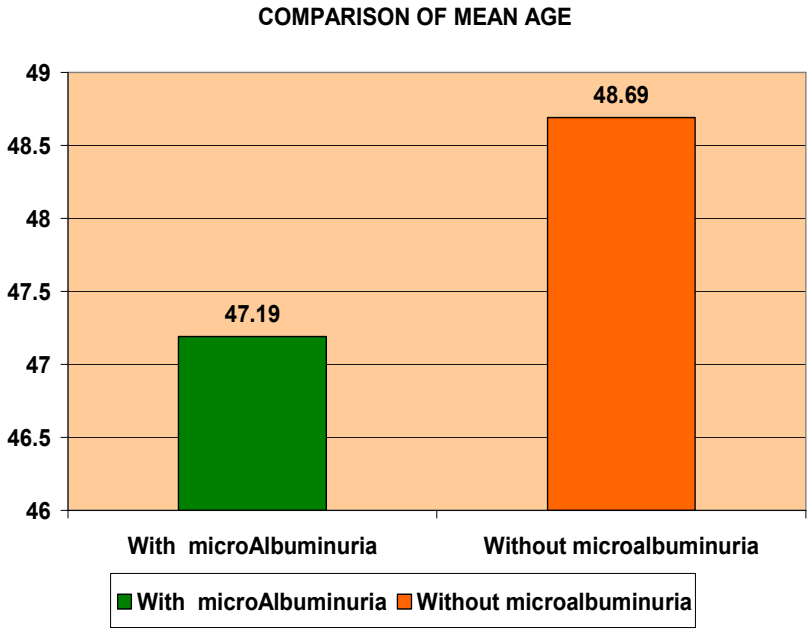
Table 11

Association of age / sex with the presence of microalbuminuria

S.No	Presenting factors	Microalbuminuria		Total (n=60)
		Absent (n = 29)	**Present (n=31)**	
1.	Age in years (Mean ± SD)	48.89.±15.23	47.19±14.03	0.128
2.	Sex	Male=21 Female=8	Male=20 Female=11	0.235
	Inference	Age and sex are not statistically associated with the presence of microalbuminuria ($p>0.05$).		

Figure 14

Association of age / sex with the presence of microalbuminuria



Of the 31 patients with microalbuminuria, 16 patients were above the age of 50 years but age was not statistically associated with presence of microalbuminuria (47.19±14.03Vs. 48.69±15.23).

Among the patients with microalbuminuria 20 were male and 11 female. Hence, gender was not statistically associated with presence of microalbuminuria.

Table 12

Mean pattern of parameters

Parameters (Mean ± SD)	**Pt with MA (n=31)**	**Pt without MA (n=29)**	**p value**
SBP mm Hg	117.36±9.83	117.48±10.32	0.961
DBP mm Hg	75.36±5.30	74.76±4.91	0.654
RBS	108.13±13.65	107.66±11.47	0.885
Blood Urea	27.16±5.23	24.40±4.19	0.021
Serum Creatinine	0.94±0.17	0.83±0.14	0.042

Figure-15

Systolic BP

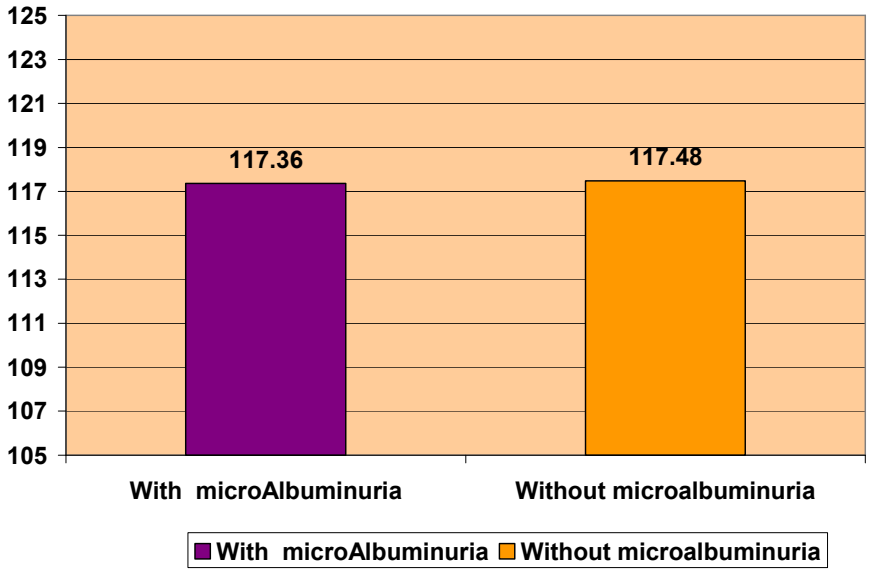


Figure-16

Diastolic BP

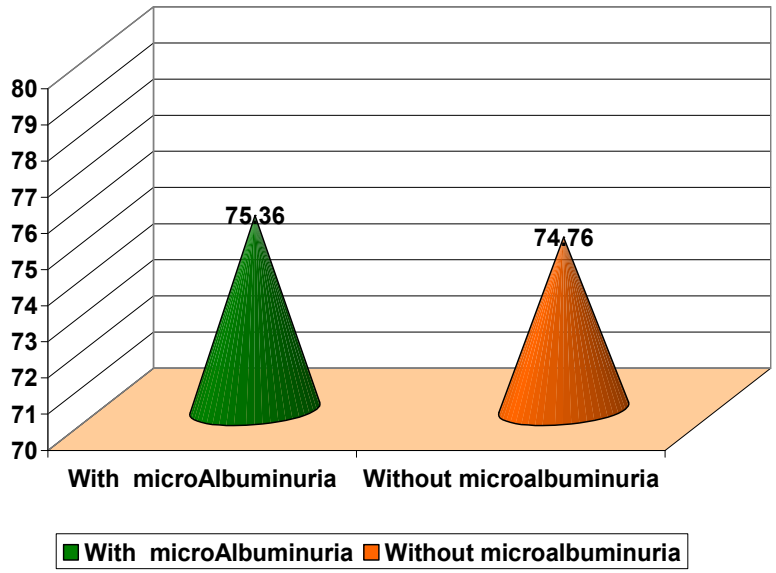
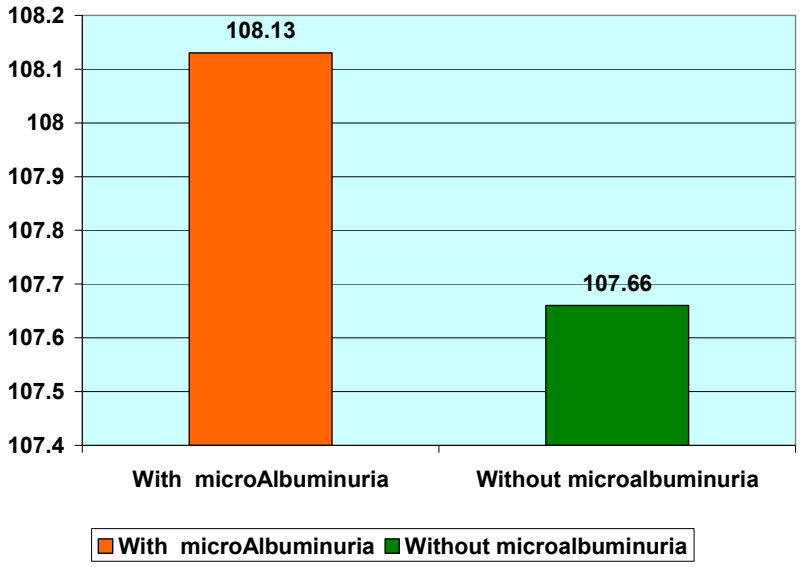


Figure-17

RBS



Blood pressure was found to be similar between patients with microalbuminuria and without microalbuminuria.

Blood Sugar was 108.13±13.65 among patients with microaluminuria while 107.66±11.47among patients without microalbuminuria and was statistically insignificant.

Among patients with microalbuminuria, blood urea was 26.56±5.01, serum creatinine was 0.92±0.15 while in patients without microalbuminuria, it was 24.10±2.99 and 0.85±0.12 respectively.

Table 13

Mean Pattern of Lipid Parameters

Parameters (Mean ±SD)	With MA (n=31)	Without MA (n=29)	p value
Triglycerides	192.45±35.59	157.93±33.49	<0.001
Total cholesterol	204.3±13.73	193.9±23.58	<0.043

Figure 18

Mean Pattern of Lipid Parameters

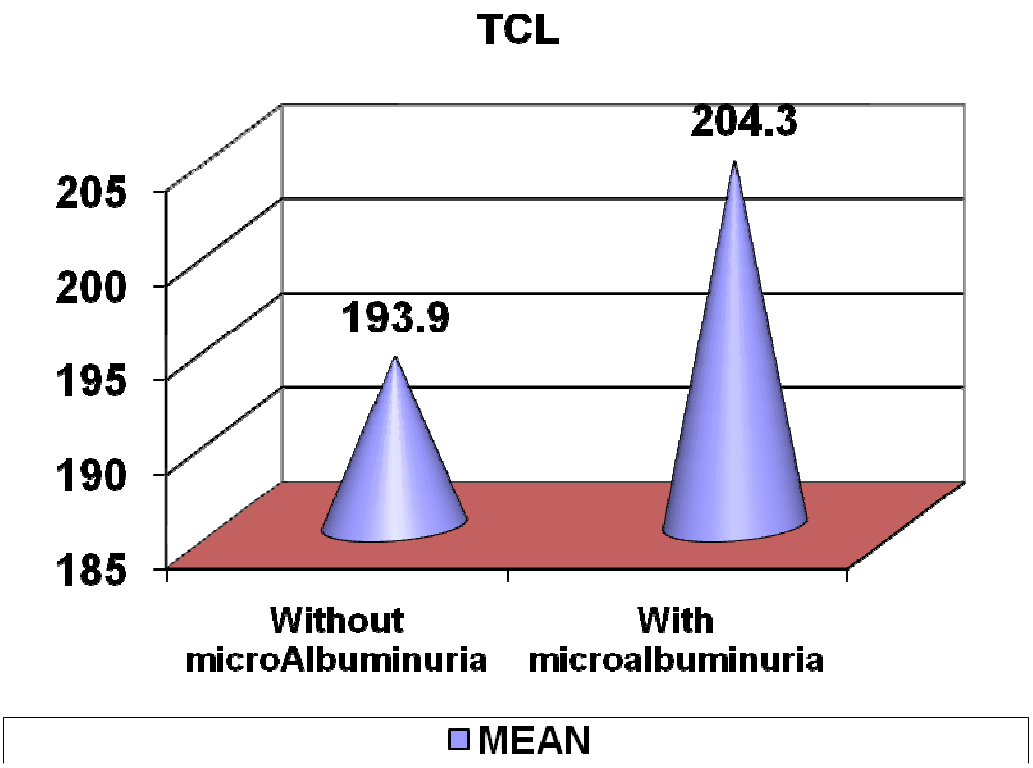
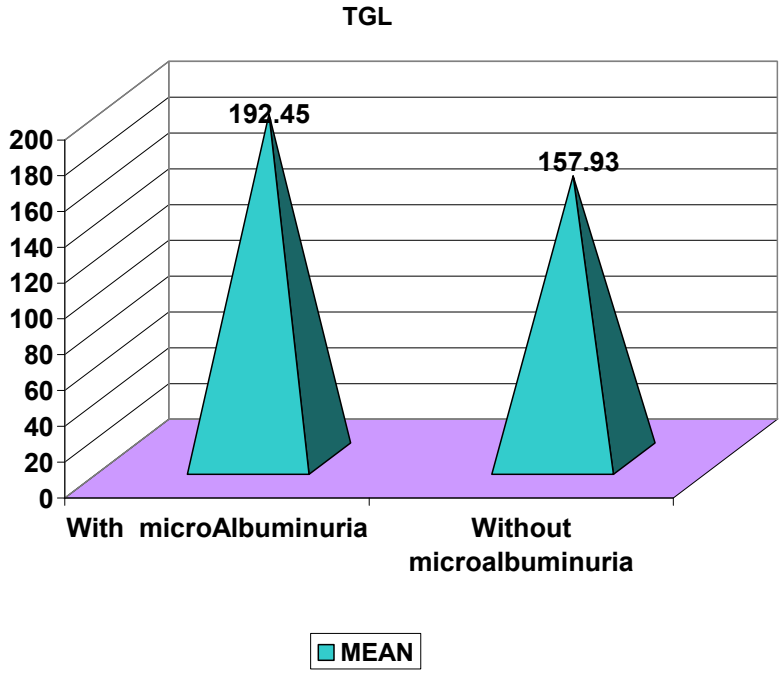


Figure-19



The fasting lipid profile showed higher trends among patients with MA than patients without MA and reaching statistically significant levels.

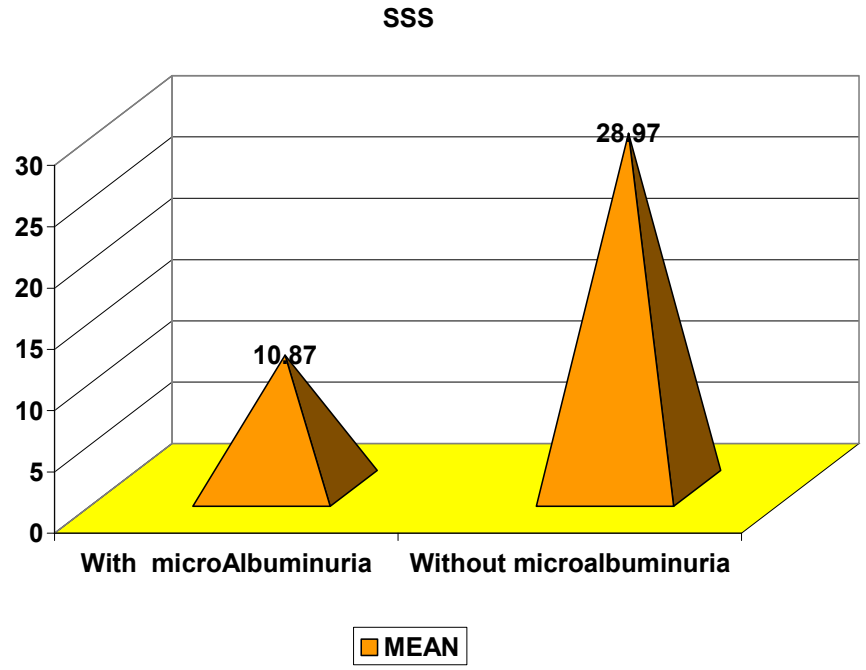
Table 14

Mean Pattern of SSS in presence of Microalbuminuria

S.No	Presenting factors	Microalbuminuria		P value
		Absent (n = 29)	Present (n=31)	
1.	Mean ±SD	10.87±2.98	28.97±8.67	<0.001
2.	95% CI	14.31-21.96	21.66-24.54	
	Inference	SSS is significantly decreased in the presence of Microalbuminuria with p<0.001		

Figure 20

Mean Pattern of SSS in presence of Microalbuminuria



The severity of stroke was assessed by Scandinavian Stroke Scale and was found to significantly lower in presence of microalbuminuria (8-19 with mean of 10.87±2.98) than without microalbuminuria (10-44 with mean of 28.97±8.67).

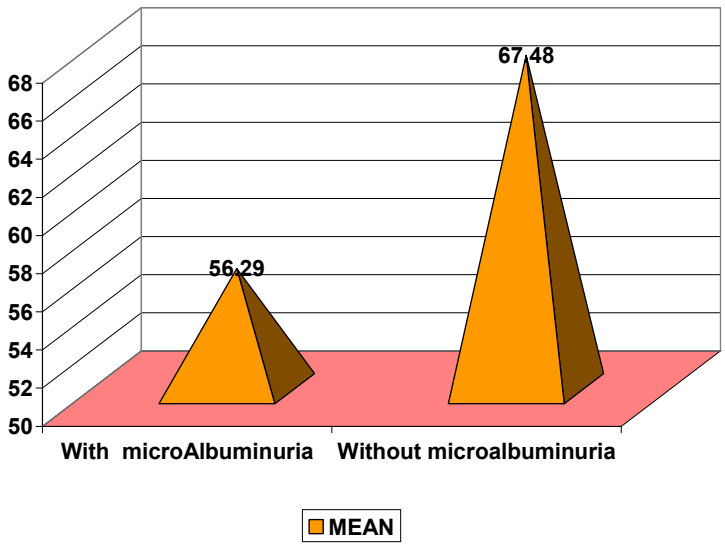
Table 15

Mean Pattern of Barthel Index in presence of Microalbuminuria

S.No	Presenting factors	Microalbuminuria		P value
		Absent (n = 29)	Present (n=31)	
1.	Mean ±SD	56.29±5.77	67.48±10.91	<0.001
	Inference	Barthel Index is significantly decreased in the presence of Microalbuminuria with p<0.001.		

Figure 21

Mean Pattern of Barthel Index in presence of Microalbuminuria



Assessment of activities of daily living by Barthel Index after 6 weeks showed that it was lower in patients with microalbuminuria (50-70) than without microalbuminuria (45-100).

DISCUSSION

The present study is a prospective study consisting of 60 recent ischemic stroke patients are divided into two categories as patients with microalbuminuria and patients without microalbuniuria.

1. The incidence of microalbuminuria in recent ischemic stroke patients.

2. The difference in laboratory parameters in patients with and without microalbuminuria.

3. The correlation between Scandinavian Stroke Scale and Barthel Index and presence of microalbuminuria.

Incidence of microalbuminuria

	Pt with MA	**Pt without MA**
Turaj et al	46.1%	13.5%
Beamer et al	29%	10%
Slowik A et al	46.7%	16.7%
Present study	51.66%	48.34%

Our study found that among age and sex matched cases with microalbuminuria and without microalbuminuria are with similar predisposing factors, patients with new stroke were 6.32 times more likely to have microalbuminuria. The finding was similar to that of other studies including Turaj et al[74], Beamer et al[71] and Slowik A et al.

Age and microalbuminuria

	With MA	**Without MA**
Turaj et al	73.3±11.6	66.0±12.4
Beamer et al	69±7	65±8
Present study	47.19±14.03	48.69 ±15.23

The studies including Turaj et al[74] and Beamer et al[71] had found statistically significant correlation and attributed this to the phenomenon of older patients having a worse neurological deficit. Our study found correlation between age and presence of microalbuminuria but it didn't reach statistically significant level. Gender and Microalbuminuria

	With MA	Without MA
Turaj et al		
Males	12 (50%)	14 (50%)
Females	12 (50%)	14 (50%)
Present study		
Males	20 (64.5%)	21 (72.4%)
Females	10(33%)	8 (22.7%)

The study did not reveal any difference in gender distribution between patients with or without microalbuminuria. This was consistent with study by Turaj et al.

Previous history of vascular events

	With MA	Without MA
Turaj et al	9 (37.5%)	16 (57.2%)
Present study	12 (16.12%)	2 (6.89%)

Present study showed statistically significant increase in previous history of vascular events. But the study by Turaj et al[74] did not find any difference between patients with and without microalbuminuria regarding previous history of vascular events. Our study is statistically significant.

Evidence of IHD and microalbuminuria

	With MA	Without MA
Turaj et al	9 (37.5%)	15 (53.6%)
Present study	8 (25.80%)	1 (3.44%)

Turaj et al[74] did not find any difference between patients with or without microalbuminuria in relation to presence of ischemic heart disease while our study found that the patients with microalbuminuria had greater evidence of IHD (25.80% Vs. 3.44%). This shows that microalbuminuria is related to all the atherosclerotic vascular events including IHD.

Loss of consciousness and microalbuminuria

	With MA	Without MA	p value
Turaj et al	35.5%	14.3%	< 0.05
Present study	38.70%	6.89%	0.043

Our study found statistically significant correlation between diminished consciousness between patients with and without microalbuminuria. The study by Turaj et al[74] also had similar findings. Hence, presence of microalbuminuria was found to correlate with the severity of stroke.

SUMMARY

1. The study population consisted of 60 recent ischemic stroke patients of age 48.69±15.20 years with 41 males (68.33%) and 19 females (31.67%).

2. The patients without microalbuminuria included 29, age and sex matched individuals.

3. The patients with microalbuminuria and without microalbuminuria were matched for predisposing factors that included smoking and alcohol.

4. Among the patients with microalbuminuria , 15 (49.39%) had right hemiparesis, 16 (51.61%) had left hemi paresis.

5. CT scan results revealed that middle cerebral artery infarct predominated the study population (right and left each 43.75%).

6. The blood sugar levels were higher in with microalbuminuria (108.66±8.683) compared to without microalbuminuria (107.83±8.21) despite being in non-diabetic range but were not statistically significant. Other parameters like blood pressure, blood urea and serum creatinine were similar among the patients with microalbuminuria and without microalbuminuria

7. In patients with recent ischemic stroke, 31 pts (51.65%) had microalbuminuria while 21 patients (49.35%) had no microalbuminuria.

8. 12/31 patients with microalbuminuria (38.70) had altered consciousness while 2/29 patients without microalbuminuria (6.89) had altered consciousness. Hence microalbuminuria was found to be associated with more severe stroke.

9. 8/31 patients with microalbuminuria (25.80) had ECG changes of ischemic heart disease while 1/29 (3.45%) patients without MA had IHD changes. Hence, microalbuminuria could be associated with not just stroke, but also other atherosclerotic vascular diseases.

10. The mean age of patients with microalbuminuria was 47.19$\pm$14.03 while that of patients without MA was 48.69$\pm$15.23 years. The difference was not statistically significant level.

11. In patients with microalbuminuria, total cholesterol was 204$\pm$13.78, and triglycerides 192.45$\pm$35.59 while in patients without microalbuminuria, total cholesterol was 193.9$\pm$23.52,and triglycerides 157.93$\pm$33.49. The difference was statistically significant.

12. The Scandinavian Stroke Scale was low in patients with microalbuminuria (7.89-13.85) when compared to patients without microalbuminuria (20.30-14). Hence significant correlation was found between microalbuminuria and the severity of the neurological deficit.

13. The Barthel index was low in patients with microalbuminuria (50-70) when compared to patients without MA (45-100). Hence, there was significant correlation between microalbuminuria and poor stroke outcome.

CONCLUSION

Various clinical studies have documented microalbuminuria as a risk factor for ischemic stroke. The present study found microalbuminuria in 51.66% of non-diabetic recent ischemic stroke patients and is consistent with previous studies associating MA with atherosclerotic vascular disease.

In the present study, We have shown that the measurement of microalbuminuria was found to be reliable predictor of stroke outcome 6 weeks after stroke.

BIBLIOGRAPHY

1. Goldstein L. Evidence – based medicine and stroke Neuroepidemiology 1999, 18; 120-124.

2. Hankey GJ, Stroke how large a public health problem and how can the neurologist help? Arch Neurol 1999; 56; 748-754.

3. Ross R.Atheroscelerosis;an inflammatory disease, N.Engl J Med 1999; 340 115 - 126.

4. Kullo IJ, Gau GJ, Tajik AJ.Novel risk factors for atheroscelerosis.Mayo Clin Pros 2000;75:369-380.

5. Hatano S.Experience from a multicentre Storke register: A Preliminary Report, Bulletin WHO 1976;54:541-43.

6. Hankey GJ.Warlow CP. Transient ischemic attacks of the brain and eye, London; WB Saunders. 1994.

7. Srinivasan AV, Balasubramanian, N.Mahesh. An Overview of Stroke – Recent Perspectives, Medicine update – APICON 2002. Editor SB Gupta 878-82.

8. Hachinski V, Norris IW. The Acute Storke. FA Davis Company, 1985.

9. Park. K.Parks Textbooks of Preventive and Social Medicine, 14th Edition Jabalpur, Banarsidas - Bhanot Publishers; 1994.

10. Devis HD et.al., Epidemiology of Cerebrovascular Disease. In Anderson D ed., Neuroepidemiology A tribute to Bruce Schoenberg Boca Raton: CRC Press 1991; 27-53.

11. Kameshwar Prasad. Epidermiology of Cerebrovasuclar Disease in India. Recent concepts in stroke. Editor B.C. Bansal: 21-27.

12. Banford J et al. A prospective study of acute cerebravascular disease in the community: The Oxfrrdshire Community Storke Project 1981-86:Methodology, demography and incident cases of the ever stroke. J Neurosurg Psych 1998; 51:1373-80.

13. Rodges A.et. al. Blood Pressure and the risk of storke in patients with cerebrovascular disease. BMJ 1996;31:147.

14. Sagie A et al. The natural history of borderline isolated systolic hypertension. N Engl J Med 1993 : 329 : 1612 – 1617.

15. Wolf PA et al. Probability of Stroke a risk profile from the Framingham study Stoke 1991: 22:312.

16. Shinton R et al. Meta analysis of relation between cigarette smoking and Stroke 1991; 22;312.

17. Jurgens G.et.al LP (a) Serum concentration and application (a) Phenotype correlate with severity and presence of ischemic cerebrovascular disease. Stroke. 1995: 26:1841-48.

18. Manson JE et al. A prospective study of maturity onset diabetes mellitus and risk of coronary heart disease and stroke in women. Arch Intern Med 1991;151; 1141-1147.

19. Jorgensen HS et al., Intracranial haemorrhage versus infarction stroke severity, risk factors and prognosis. Ann Neurol 1995:38:45-50.

20. Qizilbash N.et al. Fibrinogen and lipids as risk factor of transient ischemic attacks and minor ischemic stroke. BMJ 1991:303;605-609.

21. Qizilbash N et al. Von Willebrand Factor and risk of ischemic stroke. Neurology 1997:49:1552-1556.

22. Welin. L.et al. Analysis of risk factors for storke in a cohort of men born in 1913 N Engl J Med 1987:317:521-526.

23. Yamanouchi H et al. Embolic brain infarction in non –rheumatic atrial fibrillation: A clinicopathologic study in the elderly. Neurology 1997:48:1593-1597.

24. Wannamethee S et al. Patterns of alcohol intake and risk of stroke of stroke in middle aged British Men Stroke 1996: 27: 1033-109.

25. Kaplan NM.Alcohol and hypertension Lancet 1995; 345; 1588 – 1589.

26. Shinton R et al. Body fat and strok. J Epidemiol Community Health 1995;49: 259 – 264.

27. Ovencia AJ et al. Fish Consumption and stroke in men. Stroke 1996; 27: 204 – 209.

28. Thelle DS. Salt and blood pressure revisited. BMJ 1996; 312: 1240 – 1241.

29. Whelton PK et al. Effects of oral potassium on blood pressure. JAMA 1997:277: 1624 – 1632.

30. Lee IM et al., Exercise and risk of stroke in male physicians. Stroke 1999:30: 1- 6.

31. Kannel WB et al., Manifestations of CHD predisposing to stroke. JAMA1983; 250:2942 – 2946.

32. Craven TE et al. Evaluation of the association between carotid artery atherosclerosis and coronary artery stenosis. Circulation 1990; 82: 230-1242.

33. Natowicz M et al. Mendelian etiologies of stroke. Ann Neurol 1987: 22: 175– 192.

34. Wade S.Smith, Claiborne Johnston, Donald Easton. Cerebrovascular Diseases, Harrisons Principles of Internal Medicine. 16th ed; Vol. II 2372 – 2393.

35. Ralph L, Sacco, Danilo Toni, Mohr JP. Classification of ischaemic Stroke. Stroke Pathophysiology, Diagnosis and Management. Editor – HIM Barnett, JP Mohr, BM Stun , FM Yatsu. 3rd ed, Churchill Livingstone 1998; PP 343.

36. Pushpa Yadav, BK Tripathi, AK Agarwal, Prognostication in stroke –Recent concepts in stroke. Editor: Bansal B.C., 301-310.

37. Multicenter trial of hemodilution is ischemic stroke – background and study Protocol, Scandinavian Stroke Study Group. Stroke 1985; 16(5) :885-90.

38. Loewen SC, Anderson BA, Predictors of stroke outcome using objective measurement scales, Stroke 1990: 71 – 81.

39. Bangstad HJ, Try K, Dahl JK, Hansen KF, New Semiquantitative dispstick test for Microbuminuria, Diabetes care 1991; 14: 1094 – 1097.

40. Andrew Hartland and Peter Gostling, Microalbuminuria: Yet another cardiovascular risk factor? Ann Clin Biochem 1999; 36: 700-703.

41. Gosling P.Beevers DG. Urinary albumin excretion in the general population. Clin Sci 1989, 76:39-42.

42. Stender S.Hjelms E.In vivo transfer of Choledstrol from plasma into human aortic tissue. Scand J Clin Lab Invest 1987:47:21-29.

43. Lindberg G.Eglund GA. Gulberg B, Rastan G.Serum Sialic acid concentration and cardiovascular mortality. BMJ 1991; 302:153-161.

44. Clausen P, Jensen J, Jensen G et al. Elevated urinary albumin excretion is associated with impaired arterial dilatory capacity in clinically health subjects Circulation 2001; 103; 1869 – 1874.

45. Lee P, Jerkins A , Bourkhe C et al., Prothrombotic and antithrombotic factors are elevated in patients with type 1 diabetes complicated by microalbuminuria. Diabet Med 1993:10(2):122-128.

46. Bhattacharya A.Microalbuminuria in diabetic nephropathy and as risk factor for cardiovascular disease, Chapter 66, Medicine update. Venkatraman S 2004:14:405-409.

47. Kuusisto J, Mykkensen K, Pyorala K et al., Hyperinsulinemic microalbuminuira: A new risk indicator for coronary heart disease. Circular 1995;91(3):831-837.

48. American Diabetes Association, Nephropathy in Diabetes (Position statement) Diabetes Care 2004 ; 27 (1) : 79-83

49. Rush University Hypertension Center. Microalbuminiuria: What is Why is it important? What should be done about it? J Clin Hypertens 2001; 3(2) :99-100.

50. Parving HH et al. Early detection of patients at risk of developing diabetic nephropathy; a longitudinal study of urinary albumin excretion. Acta Endocrinal (Copenti) 1982; 100:550-55.

51. Viberti GC, Hill RD, Jarpet RJ et al., Microalbuminuria as a predictor of clinical nephropathy in Insulin Dependent Diabetics Mellitus. Lancet 1982; 1: 1430 – 1432.

52. Mogensen CE. Microalbuminuria predicts clinical proteinuria and early Mortality in maturity onset diabetics. NEJM 1984; 310:350-60.

53. Allawi J, Jarrett R.J. Microalbuminuria and Cardiovascular risk factors in Type 2 diabetics mellitus. Diabetes Med 1989; 7:115-118.

54. Jorge L, Gross et al. Diabetic Nephropathy: Diagnosis Prevention and treatment Diabetes. Diabetes care 1999:21:1551-68.

55. Consensus development Agarwal B et al. Microalbuminuria screening by reagent strip predicts cardiovascular risk in hypertension. J.Hypertension 1996;14(2):223 – 228.

56. Dansgaard EM et al., Microalbuminuria as predictor of increased mortality in elderly people. BMJ 1990:200:297-300.

57. Gostling P, Hughes EA, Reynolds TM, Fox JP. Microalbuminuria is an early response following acute myocardial infarction. Eur Heart J 1991; 12:508-513.

58. Spyridon Kouloruis et al. Microalbuminuria: A strong predictor of 3 – year Adverse prognosis in non – diabetic patients with acute myocardial infarction. Am Heart J 1991; 12:508 – 513.

59. Roine I Microalbuminuria:an index of severity in childhood meningitis. Pediatr Infect Dis J 1993; 12:584-588.

60. Shearman CP, Gosling P, Walker KJ. Is low – level protein urea a predictor of severity in acute pancreatitis? J Clin Pathol 1989; 42:1132-1135.

61. Pallister I, Gosling, P, Alpar K, Gradley S. Prediction of Post – traumatic adult respiratory distress syndrome by albumin excretion rate eight hours after admission. J.Trauma 1997; 41 : 1056-61.

62. Pederson LM et al Microalbuminuria in patients with rheumatoid arthritis. Ann Rheum Dis 1995 ; 54 : 189 – 192.

63. Mahmood N.et al. Microalbuminuria : a disease activity marker of inflammatory bowel disease, Gut 1993; 34:524.

64. Hickey NC et al., Effect of surgery on the systemic inflammatory response to intermittent claudication Br.J.Jurg 1009; 77; 1121-1126.

65. Mykkanen L et al. Microalbuminuria and carotid artery intima – media thickness in non – diabetic and NIDDM subjects. The Insulin Resistance Atherosclerosis Study (IRAS). Stroke 1997; 28;1710-1716.

66. Else Marie Damsgaard et al., Microalbuminiria as predictor of increased morality in elderly people. BMJ 1990; 300:297 – 300.

67. JohnS.Yudkin et al., Microalbuminuria as predictor of vascular disease in non – diabetic subjects. Lancet 1988; 530 533.

68. Heikki Miettinen et al., Proteinuira Predicts stroke and other atherosclerotic vascular disease events in non-diabetic and non – insulin dependent diabetic subjects. Stroke 1996; 27:2033-2039.

69. Mlacak B.et al., Albuminuria, Cardiovascular morbidity and mortality in diabetic and non – diabetic subjects in a rural general practice. Family Practice 1999; 16: 580-585.

70. Nancy B. Bearner et al., Microalbuminuria. In ischemic stroke Arch Neurol 1999; 56: 699 – 702.

71. Yuyun MF et al., Microalbuminuria and stroke in a British Population: the European Prospective Investigation into cancer in Norfolk (EPIC – Norfolk)

72. Population study. J Intern Med 2004; 255(2): 247 – 256.

73. Hans L.Hillege et al., Microalbuminuria is common, also is a non – diabetic ,non – hypertensive population and an independent indicator of cardiovascular risk factors and Cardiovascular morbidity, J. Intern Med 2002: 249::519-526.

74. Wojeiech Turaj et al., The prognostic significance of microalbuminuira in non diabetic acute stroke Patients. Med Sci Monit 2001; 7(5): 989 – 994.

75. Keen H, Chloverakis C. An Immunoassay method for urinary albumin at low concentration. Lancet 1963; 2 :913-914.

76. Alfredo Pegoraro et al., Simplified screening for Microalbuminuria. Ann Intern Med 1997; 127 : 817 – 819.

77. Magensen CE et al., Multicenter evalution of the Micral – Test II test strip, an Immunological rapid test for the detection of microalbuminuria. Diabetes cares 1997; 1642 – 1646.

78. Wachtell K et al., Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy. The LIFE STUDY. Ann Intern Med 2003; 139: 901 – 906.

79. UK Prospective Diabetes Study (UKPDS) Group intensive blood glucose control with Sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. Lancet 1998:352:837 – 853.

80. 80. Smulders YM et al., Can reduction in hypertriglyceridemia slows progression of microalbuminuria in patients with NIDDM. Eur J Clin Invest 1997:27(12) 997 – 1002.

81. Radrigo Tagle, Monico Acevedo, Donald G. Vidt. Micro albuminuria : Is it a valid predictor of cardiovascular risk. Cleveland Clin J Med 2003; 70(3): 255 – 261.

82. Slowik A et al., Microalbuminuria in non- diabetic patients with acute ischemic storke: Prevalence, clinical correlates and prognostic significance.

ANNEXURE-1

PROFORMA

Name of the patient

Age

Sex

IP No

DOA

DOD

PRESENTING COMPLAINTS:

Onset

Mode

Time

March of events

Headache

Vomiting

State of consciousness

Convulsions

Speech disturbances

Hemiparesis/Hemiplegia

Hemianesthesia

Bladder/bowel disturbances

Cranial nerve involvement

Visual disturbances

Unsteadiness of gait

Giddiness

PAST HISTORY

Diabetes

Hypertension

TIA

Previous CVA

IHD

Claudication

Atrial fibrillation

Tuberculosis

TREATMENT HISTORY

PERSONAL HISTORY

Tobacco chewing

Smoking

Alcohol

FAMILY HISTORY

GENERAL PHYSICAL EXAMINATION

Built

Nourishment

Ht

Wt

BMI

Vitals- pulse

BP

RR

Temperature

SYSTEMIC EXAMINATION

CENTRAL NERVOUS SYSTEM

Handedness

HMF

Level of consciousness

Appearance

Orientation

Memory

Intelligence

H allucination/Delusion

Speech

Cranial nerves

Motor system

Nutrition

Tone

Power

Reflexus

Sensory system

Touch

Temperature

Pain

Position sense

Vibration sensation

Cortical sensation

Rombergs sign

Cerebellar signs

Signs of meningeal irritation

Other system

CVS

RS

ABDOMEN

CLINICAL DIAGNOSIS

INVESTIGATIONS

Complete blood count

RBS

Blood urea/Sr.cratinine

ECG

Lipid profile

CT brain

LFT

Urine microalbuminuria by micral test

FINAL DIAGNOSIS

TREATMENT GIVEN

FOLLOWUP DETAILS

INFORMED CONCENT

DEPARTMENT OF GENERAL MEDICINE

COIMBATORE MEDICAL COLLEGE,COIMBATORE

Principle investigator: Dr. M. Kavitha

Research guide : **Prof. Dr. C. MANOKARAN. M.D**

Organitation : Department of General medicine

Informed consent : I have been invited to participate in research project titled

"A STUDY OF PROGNOSTIC SIGNIFICANCE OF MICROALBUMINURIA IN NONDIBETIC PATIENTS WITH RECENT ISCHEMIC CEREBROVASCULAR STROKE"

I understand it will answering a set of questionnaire, undergo physical examination, basic investigations and appropriate treatment. I also give consent to utilize my personal details for study purpose and can be contacted if necessary. I am aware that I have the right to withdraw at any time which will not affect my medical care.

Name of the patient;

Signature:

Date:

ஒப்புதல் படிவம்

பெயர் :

பாலினம் : வயது :

முகவரி :

அரசு கோவை மருத்துவக் கல்லூரியில் மகப்பேறு மருத்துவ துறையில் பட்ட மேற்படிப்பு பயிலும் மாணவி அவர்கள் மேற்கொள்ளும் **"சர்க்கரை நோய் அல்லாத, சமீபமாக மூளை இரத்த நாளங்கள் அடைப்பால் பாதிக்கப்பட்டவர்களின் சிறுநீரில் நுண் புரதத்தின் அளவு கொண்டு நோய் குணமாதலின் முக்கியத்துவம்**" குறித்த ஆய்வில் செய்முறை மற்றும் அனைத்து விவரங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்திக் கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

நான் இந்த ஆய்வில் முழு சம்மதத்துடன், சுய சிந்தனையுடனும் கலந்து கொள்ள சம்மதிக்கிறேன்.

இந்த ஆய்வில் என்னுடைய அனைத்து விபரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதை தெரிவித்துக் கொள்கிறேன். எந்த நேரத்தில் இந்த ஆய்விலிருந்து நான் விலகிக் கொள்ள எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இடம் : கையொப்பம் / ரேகை

நாள் :

KEY TO MASTER CHART

MA	-	microalbuminuria
LFT	-	liver function test
RBS	-	random blood sugar
TCL	-	total cholesterol
TGL	-	triglyceride
PVE	-	previous vascular event
SSS	-	scandinavian stroke scale
BI	-	Barthel index
L	-	left
R	-	right
M	-	male
F	-	female
IHD	-	ischemic heart disease

S.No	Name	IP No.	AGE	SEX	PRESENTING COMPLAINTS						PAST HISTORY				PRESENT HISTORY					LIPID PROFILE BP							
					WEAKNESS	HEAD ACHE	LOSE OF CONCIOUS	VOMITING	APHASIA	SEIZURES	H/O PVE	DM	SHT	IHD	ALCOHAL	SMOKE	UREA	CREATININE	LFT	RBS	TCL	TGL	SBP	DBP	CT BRAIN	MA	SSS	BI
1	RAJAN	10201	39	M	R			-	P							P	18	1.2	N	122	235	118	110	70	L	P	8	50
2	MUTHULAKSHMI	11231	41	F	R			-	P		P			P			28	0.8	N	128	230	255	110	70	L	P	9	55
3	VASANTHAPRIYAN	43541	19	M	L			-							P	P	34	1.1	N	100	200	182	116	72	R	P	10	60
4	BLAJI	44412	43	M	L			-									27	1.4	N	102	195	190	114	74	R	P	8	55
5	KANIMOZHI	23234	24	F	L		P	-									29	1.7	N	95	155	200	110	72	R	P	12	65
6	SENKOTTAYAN	54586	45	M	L		P	-							P	P	36	0.9	N	97	162	201	100	70	R	P	16	60
7	MURALI	57301	27	M	L			-								P	44	0.9	N	99	175	165	132	82	R	P	18	65
8	MOIDEEN	50501	47	M	R		P	-			P			P	P	P	35	1.4	N	102	182	117	130	84	R	P	19	70
9	JAMES	10586	51	M	R			-									37	1.3	N	126	193	112	100	74	L	P	10	55
10	MARIYAMMAL	10593	53	F	R		P	-									26	1.6	N	120	197	205	126	80	L	P	12	55
11	PALANISAMY	11731	62	M	L		P	-			P			P	P	P	36	1.3	N	111	205	223	124	80	R	P	10	50
12	PODUM PONNU	11926	65	F	L		P	-			P						27	1.4	N	115	225	215	130	82	R	P	8	50
13	ARIVAZHAGAN	11954	53	M	L			-			P			P	P	P	29	1.2	N	87	225	219	126	84	R	P	17	65
14	MUSTHAFA	40526	55	M	R			-	P						P	P	30	1.3	N	95	196	216	124	74	L	P	8	50
15	GEETHA	31264	64	F	R		P	-	P		P			P			20	1.3	N	96	187	225	124	76	L	P	9	55
16	ELANGO	35352	29	M	L			-								P	38	1.4	N	117	147	127	120	70	L	P	10	60
17	PETCHIYAMML	50123	49	F	R			-									29	1.5	N	118	165	155	110	84	L	P	11	55
18	NATARAJAN	45621	57	M	L		P	-			P			P	P	P	37	1.2	N	117	167	167	110	70	R	P	12	60
19	NANDHAKUMAR	57281	30	M	L			-			P				P	P	35	1.2	N	122	171	165	130	78	R	P	10	55
20	SELVI	9545	59	F	R		P	-	P	P	P			P			39	0.9	N	126	179	200	130	84	L	P	9	55
21	MARIMUTHU	10643	50	M	L			-							P	P	40	0.8	N	115	205	208	128	70	R	P	8	50
22	MUNIYAMMAL	12191	40	F	R			-						P			27	1.4	N	97	223	209	120	70	R	P	9	50
23	RAJASEKARAN	20243	52	M	R			-	P							P	38	0.6	N	87	202	225	110	70	L	P	10	60
24	RATHNAM	56573	32	M	R			-			P				P	P	33	0.9	N	95	204	215	110	68	L	P	11	60
25	KARTHIKEYAN	55551	35	M	L			-								P	21	1.2	N	112	215	216	114	80	R	P	13	60
26	MURUGAN	57891	51	M	L		P	-									29	1.4	N	119	219	217	100	70	R	P	12	65
27	VISALATCHI	44561	54	F	L			-								P	25	1.3	N	78	211	219	110	72	R	P	8	50
28	VIRUMANDI	44563	58	M	L			-			P					P	29	1.2	N	95	159	195	110	74	R	P	10	50
29	SENBAGAVALLI	38492	77	F	R		P	-	P		P						66	1.3	N	116	187	198	110	74	L	P	11	55

30	SUBRAYAN	39415	69	M	R		P	-							P	P	34	1.3	N	119	190	197	120	78	L	P	11	50
31	SARASWATHI	38145	33	F	R			-							P	P	29	1.3	N	124	205	210	130	80	L	P	8	50
32	KARUPPAYAH	40561	42	M	R				P						P		28	1.2	N	98	200	198	110	70	L	-	30	70
33	ARUKKANI	47245	51	F	L												24	1.4	N	95	215	150	114	72	R	-	32	75
34	JEGADEESAN	46489	21	M	L												45	0.9	N	110	217	160	122	72	R	-	35	70
35	SHANTHANAM	50676	40	M	R												44	0.8	N	115	198	202	130	70	L	-	31	70
36	DAVID	50129	35	M	L										P	P	46	0.9	N	120	187	216	110	70	R	-	26	65
37	MAHENDIRAN	42819	25	M	R										P		23	1.3	N	112	210	195	100	70	L	-	28	60
38	PRABHAKARAN	62048	51	M	R				P						P		24	1.4	N	125	210	145	102	72	L	-	44	100
39	MAYILSAMY	49955	65	M	L												35	1.2	N	92	196	175	110	74	R	-	35	70
40	LATHA	45214	69	F	L												33	1.3	N	80	225	185	120	80	R	-	30	70
41	NARAYANAN	44616	45	M	R				P						P	P	65	1.2	N	110	150	98	130	82	L	-	26	65
42	KATHIRVEL	32814	68	M	L				P	P	P				P		44	1.3	N	114	146	125	132	80	R	-	28	60
43	CHELLADURAI	21119	53	M	R												34	1.3	N	92	210	200	139	80	L	-	28	60
44	RAJAJI	21189	65	M	L												28	1.4	N	98	213	198	124	80	R	-	29	65
45	RAKKU	51004	47	F	R				P								29	1.5	N	100	190	200	122	82	L	-	15	60
46	SIVANANDI	45555	83	M	L	P	P								P		26	1.3	N	114	185	205	120	84	R	-	12	50
47	MARIYAPPAN	45819	28	M	R												27	0.9	N	115	170	140	110	80	L	-	25	57
48	ARAYEE	43108	54	F	L												28	1.3	N	113	175	130	112	70	R	-	26	60
49	SUBRAMANIYAN	53916	36	M	R										P	P	25	0.8	N	103	190	140	110	70	L	-	13	50
50	KUPPAMMAL	57819	59	F	B/L												22	0.9	N	118	210	150	100	70	CL	-	10	45
51	SEVALAI	52312	29	M	L										P	P	21	0.7	N	94	225	155	122	72	R	-	30	70
52	POONKODI	63016	56	F	L		P										29	0.9	N	95	204	150	130	74	R	-	42	80
53	SUNDHAR	57192	62	M	L				P					P	P		28	0.9	N	96	208	135	136	76	R	-	41	80
54	VIJAYAKUMAR	48912	39	M	R						P						24	1.3	N	114	225	120	110	70	L	-	40	80
55	THIRUMAL	48197	26	M	L											P	33	1.4	N	125	224	110	110	70	R	-	39	80
56	SARANYA	33121	54	F	R												36	1.2	N	120	210	112	120	82	L	-	38	70
57	SIKENDAR	34532	48	M	R	P											44	1.3	N	118	188	120	122	80	L	-	25	65
58	DHANALAKSHMI	40011	54	F	L												22	1.3	N	116	114	150	110	70	R	-	28	70
59	MAHALINGAM	47111	42	M	R				P								25	1.3	N	114	196	144	114	72	L	-	28	70
60	MUTHUMARI	49122	65	M	R				P								23	1.2	N	106	192	172	116	74	L	-	26	70